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ANNALS *of* SURGERY

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TRAUMATIC RUPTURE OF THE INTESTINES CAUSED BY AUTOMOBILE ACCIDENTS *

By H. Hamilton Cooke, M.D

of Lowville, New York

Although numerous agents can cause traumatic rupture of the intestines, only a few cases have been described as the result of automobile accidents. My purpose in this study is to present the clinical and necropsy observations in twelve cases of traumatic rupture of the intestines caused by automobile accidents. The necropsy in these cases was made at the Department of Pathology, University of Minnesota, between December 1, 1919, and December 1, 1929.

The cases under consideration have been divided into two groups: (1) Those in which death occurred primarily from the effects of general trauma, and (2) those in which the general trauma was relatively slight and death was due to the rupture of the intestines.

The first group (Table I) was composed of ten males and two females. Three of the male and one of the female subjects were less than fifteen years of age. The lesions were in the duodenum in two cases, at the duodenal-jejunal flexure in one case, in the jejunum in six cases, in the ileum in two cases, and in the ascending colon in one case. Multiple rupture of the intestines was not observed.

Two cases of rupture of the ileum and one case of rupture of the jejunum were associated with rupture of the stomach. The intestinal loop was completely severed in three cases and almost severed in one case; in eight cases the rupture varied in diameter from five to fifteen millimeters. Free blood was present in the peritoneal cavity in eleven cases. The quantity varied from 250 to 2,000 cubic centimetres. In two cases, the rupture of the intestine was associated with injury to the liver, spleen and kidneys, in two cases with injuries to the liver and spleen and in one case with injury to the pancreas. The mesentery was cut across in one case, lacerated in two cases, and infiltrated with blood in two cases. The quantity of blood found free in the peritoneal cavity appeared to vary with the degree of injury to the liver, spleen, mesentery and pancreas. General fibrinopurulent peritonitis occurred in four cases in which the patients lived forty-eight, forty, and thirty-eight hours after injury.

* Work done at the Department of Pathology, University of Minnesota, while a Fellow in Surgery of The Mayo Clinic.

Quain, in 1921, reported the case of a girl aged fifteen years, who was thrown from an automobile. An operation was performed forty hours after the injury. Two small perforations in the jejunum, two centimetres from the duodeno-jejunal juncture, were closed with sutures of linen and catgut. After a stormy convalescence the patient recovered completely.

Vance, in 1923, reported two cases: One, in which a male, aged fifty-seven years, was run over by a motor truck. He was unconscious for about seven hours and died about nine hours after the accident. Necropsy disclosed a hole, four centimetres in diameter, in the middle of the omentum, a partial tear across the duodenum, and a complete tear of the jejunum, three feet from the duodenojejunal juncture. The second case was that of a man, aged twenty-nine years, who was struck by a motor truck. He was taken to a hospital and exploratory laparotomy was performed. A tear in the jejunum was sutured. The patient died of peritonitis several hours later. At necropsy, a complete transverse rupture of the jejunum was found forty-five centimetres from the duodenojejunal juncture. There was also a large contusion in the mesentery in the region of the intestinal injury. In 1928, Vance described two additional cases in which operation was performed. One of the patients recovered.

Bacon and Le Count have recently reported the necropsy observations in 303 cases of accidental death. Rupture in the intestine, due to automobile accidents, was found in nine cases. In one case, the rupture was in the transverse portion of the duodenum. The jejunum and mesentery were torn in three cases. The ileum was lacerated in four cases. One patient in this group lived for eighteen hours after the accident. A serious injury to the peritoneal viscera was suspected in one case, and exploration disclosed rupture of the colon. This was closed, but the patient died eight days later from general peritonitis.

In six cases, in addition to the intestinal injury, the severe general trauma caused death either immediately or very soon after the accident. Only three of these six patients reached the hospital alive. An injury to the intestine was not suspected, and the rupture was found only at necropsy. In the six other cases, the rupture of the intestine constituted the principal injury. The patients lived from nine to forty-eight hours, and died primarily from intraperitoneal hæmorrhage or peritonitis.

In general, the diagnosis of rupture of the intestine from automobile accidents depends largely upon the history and upon the observation of local and general signs and symptoms of an injury to the abdominal viscera. The history is of great importance. Care should be taken in noting the character of the accident. A passenger in an automobile which is stopped suddenly may sustain an injury of the intestine by being thrown against the seats inside the automobile. In one case, the patient was riding in the back seat of a light automobile when it collided with a street car. The patient was thrown forward and struck the anterior abdominal wall against the front seat. At necropsy, a large rupture was found on the anterior surface of the proximal portion of the duodenum.

The early signs and symptoms may be due to shock, rupture of the intestine, or intraperitoneal hæmorrhage. The degree of shock varies with the amount of general trauma. In the presence of slight general trauma, rupture of the intestine may produce few immediate symptoms. The patient may even be about for a short time without realizing the gravity of the condition. In ten of the twelve cases, the shock was slight in one case, moderate in one case, and severe in eight cases.

TABLE I

Twelve Cases of Rupture of the Intestines Caused by Automobile Accidents. Death Caused by General Trauma

Case	Sex	Age	Abrasion on wall of abdomen	Duration of life; hours	Site of rupture	Size of rupture	Injury to stomach	Major associated lesions	Intraperitoneal hemorrhage -- cc --
7	M	45	None	1	Jejunum	Transverse		Subarachnoid hemorrhage tears in liver, kidneys left lung. Laceration of mesentery	300
8	F	12	Marked	1	Jejunum	Transverse	Rupture on greater curvature	Tears spleen, liver and hemo-thorax	250
9	M	23	Slight	1	Ileum	1.5 cm.	Rupture 4 cm. lesser curvature	Tears spleen, liver kidneys; fracture of skull.	1500
10	M	13	Moderate	1	Duodenum	Transverse		Tears spleen, liver pancreas.	1500
11	M	5	Slight	2 ½	Jejunum	3.5 cm.		Fracture skull	400
12	M	65	None	3	Ileum	4.5 cm.	Rupture 5.5 cm. anterior wall near pylorus	Tears in spleen Hemo-thorax	300

In seven cases the skin over the abdomen did not show any abrasions, lacerations or wounds. (Table II.) Superficial bluish discoloration over the inguinal region was present in three cases; multiple superficial abrasions of the anterior abdominal wall were present in one case, and marked lacerations with deep wounds were present in one. Of the seven cases in which the walls of the abdomen did not show any evidence of injury, the intestinal rupture was transverse in two cases and partial in five.

By means of röntgenograms of the abdomen by the flat plate method, it is possible to determine immediately after the injury the presence of free blood, intestinal contents and excessive air in the peritoneal cavity. Such röntgenograms should be taken in every case in which symptoms are sug-

TABLE II

*Death Caused by Rupture of Intestines**

Case	Sex	Age	Duration of life in hours	Site of Rupture	Size of Rupture	Major Associated Lesions	Amount of Intraperitoneal Hemorrhage	Peritonitis
1	M	58	7	Jejunum	1.5 cm.	Fractured Pelvis	2,000 c.c.	
2	M	24	15	Ascending colon	7	Fractured Pelvis Laceration of Mesentery	400 c.c.	
3	M	7	38	Jejunum	.5 cm.	Fractured Pelvis	100 c.c.	Present
4	F	51	40	Duodenum	.8 cm.		900 c.c.	Present
5	M	39	40	Jejunum	Transverse	Fractured ribs Laceration of Mesentery		Present
6	M	55	48	Jejunum	7	Laceration of Mesentery	100 c. c.	Present

* Abrasions were not found on the abdominal wall in any case.

gestive of an intra-abdominal injury. The plate should, if possible, be made with the patient in a standing position. If the injury is associated with moderate or severe shock, board-like rigidity of the abdominal wall with rebound tenderness, increased tympany over the umbilical region, absence of dullness over the liver, and rectal tenderness, a presumptive diagnosis of intestinal rupture is justified and laparotomy should be performed as soon as possible.

The observations made in the twelve cases of rupture of the intestines caused by automobile accidents noted here are compared with the observations reported in the literature of rupture of the intestines in which the automobile was not designated as the etiological factor. (Table III.)

Since 1761 there have been reported in the available literature about 700 cases of traumatic rupture of the intestines. Primary rupture of the intestines may occur by crushing, tearing and bursting from increased pressure within the lumen. Secondary traumatic rupture of the intestines follows injury to the blood supply with localized gangrene and eventual perforation. Moty (1890) was the first to clearly classify the various types of traumatic

TABLE III

Rupture of the Intestines Not Caused by Automobile Accidents

		Cause of Accident						Location of Rupture					Extent of Rupture			*Without surgical therapy	With surgical therapy		
Reporter	No. Cases	Run over by vehicle	Crushed	Kicked by horse, cow or man	Blow	Fall	Miscellaneous	Duodenum	Jejunum	Ileum	Small intestine	Colon	Transverse	Partial	Multiple	No. died	No. operated on	No. recovered	No. died
Poland (1858)	61	9		11			41	4	14	16	22	5				61			
Curtis (1887)	116	13		28	29	13	4	6	44	38	21	4	20	96	11	104	12	0	12
Makins (1899)	21	5	3	6	1	4	2	1	6	7	2	5	2	17	2	6	15	3	12
Angerer (1900)	31															12	9	3	
Gage (1902)	85															45	40	17	23
Berry (1908)	132	51	24	16	23	11	7	26	32	32	25	10				48	84	17	67
Tschistosserdorf (1912)	52			16	9	11	16	1	23	25		3				5	47	8	39
Battle (1919)	215	74	25	28	35	27	26	32	111	59	2	11					124	48	76
Rowland (1923)	381							23	157	158		43			38				
Massie (1923)	34	16	7	2	6	1	2	4	14	8	3	1	9	20	5	3	31	7	24
Moynihan (1926)	17																17	3	14

*There were no recoveries in this group

intestinal rupture. Many forms of violence have been described as the cause of intestinal rupture. The older reports of Poland (1858), Curtis (1887), and Petry (1896) emphasized that the injury is most frequently due to a kick by a horse, cow, or man, and "run-over" accidents. The increase in the number of automobiles and frequency of automobile accidents, especially in the cities of this country, directs attention to the possibility that a large number of traumatic ruptures of the intestines occur in serious or fatal automobile accidents, although only a few cases are reported in the literature. In this report, intestinal rupture occurred in more than 5 per cent. of 210 fatal automobile accidents. The rupture appears to have been caused by crushing of the intestines in four cases and tearing of the intestines in eight cases.

In considering the individual cases in relation to the effect of the injury, they seem to divide themselves into two groups. In the first group, composed of six cases, subarachnoid hæmorrhage, crushing of the chest with hemothorax, laceration of the spleen, liver, kidneys and pancreas caused almost instantaneous death. The second group is composed of six patients who lived from seven to forty-eight hours after the accident. From the viewpoint of diagnosis and therapy, this is the most hopeful and therefore the most important clinical group.

Exploratory laparotomy was performed in only one case. A rupture in the ascending colon was found and sutured. Death from peritonitis occurred, however, fifteen hours later. In the other five cases a diagnosis of rupture of the spleen was made in one case, while in another the symptoms were so slight that medical attention was not sought until more than twenty-four hours after the accident.

Moynihan believes that exploratory laparotomy is justified in all cases where a rupture of the intestines is suspected, provided vomiting continues after a period of shock, and if the pulse-rate continues to increase. Lund emphasizes the early absence of serious symptoms. He recommends exploratory laparotomy in all cases of suspected traumatic intestinal rupture, without waiting for an absolutely definite diagnosis. If there is no hæmorrhage, or only a slight one from the mesentery and the margins of the rupture, the symptoms are produced by the escape of intestinal contents into the peritoneal cavity. Douglas considers early exploratory laparotomy indicated in all cases of severe abdominal injuries. "Then, in conclusion, in all cases of subperitoneal visceral injury, diagnosed or strongly suspected, if the general condition of the patient permits, laparotomy should be done; and success will be in direct proportion to the promptness of the intervention." Van Hooke and Kanavel consider exploratory operation necessary in every suspected case of intestinal rupture where proper facilities are available.

The pre-operative treatment is of great importance and should be directed to combat shock and hæmorrhage. The patient should be kept comfortable by warm blankets and hot-water bottles. Hypodermoclysis of .9 per cent. solution of physiological saline is of value. If the patient presents evidence of shock, blood transfusion should be done before the operation. After the

rupture is located and all bleeding points on the mesentery ligated, additional fluid can be administered by the intravenous route. Without early surgical therapy, death is inevitable. All of the 118 cases collected by Curtis proved fatal. In the series of Gage and Berry, all of the patients who were not operated upon died.

In four of the cases in this report in which the patients died from peritonitis, the lesion was found in the duodenum in one case, in the jejunum in three cases, and in the colon in one case. In the twenty-six cases of rupture of the intestines in automobile accidents reported by Quain, Vance, Bacon and Le Count, and myself, nineteen of the patients were not operated on. They died from shock, hæmorrhage or peritonitis. Operations were performed in seven cases, with two recoveries and five deaths. Reliable deductions are difficult to make from a small number of cases, but it appears clear that even with adequate early surgery the mortality rate is high.

Successful surgical therapy is influenced by many factors. The most important of these are: the degree of shock; the size of the lesion; the time elapsed after injury; the amount of hæmorrhage; the site of the lesion; the condition of the mesentery, and the presence of peritonitis. Rupture of the intestines should be considered as a possibility during the examination of all persons who have sustained an abdominal injury in automobile accidents. Since surgical therapy offers the only hope for recovery in rupture of the intestines, exploratory laparotomy is imperative.

SUMMARY

Twelve cases of traumatic rupture of the intestines were found in 210 victims of automobile accidents who came to necropsy at the Department of Pathology, University of Minnesota, between December 1, 1919, and December 1, 1929. The site of the rupture was as follows: Duodenum, three cases; jejunum, six cases; ileum, two cases; ascending colon, one case. In three cases the rupture of the intestines was associated with rupture in the stomach. In three cases the rupture was transverse and in one case nearly transverse, while in eight cases the size of the rupture varied from five to fifteen millimeters in diameter. The liver, spleen, kidneys or pancreas were injured in five cases. In seven cases there were no abrasions of the skin or any external evidences of injury to the abdomen. In four cases there were a few superficial abrasions, while severe lacerations of the wall of the abdomen were found in only one case.

Free blood in the peritoneal cavity was present in eleven cases. Peritonitis was present and the principal cause of death in four cases. In six cases (50 per cent.), death occurred within one hour after the injury was received. In this group the rupture of the intestines was associated with rupture of the spleen, liver, pancreas, kidneys, fracture of the skull, subdural hæmorrhage, multiple fracture of the ribs, and hemothorax. The result of therapy in this group is discouraging. In the other six cases, the rupture of the intestines was the most serious injury and with its complications was the cause of death. The symptoms and signs were identical with

those present in traumatic rupture of the intestines from other causes than automobile accidents. The duration of life was from seven to forty-eight hours after the accidents occurred. Death was the result of peritonitis in five cases, and from peritonitis and bronchopneumonia in one case. Exploratory laparotomy was performed on only one individual. Rupture of the intestines should be considered as a possibility, whenever a person has received a severe blow on the abdomen in an automobile accident. Lacerations and wound of the wall of the abdomen are infrequent, and their absence is not a reliable criterion for the condition of the intestines, viscera, or mesentery. Early exploratory laparotomy should be performed, when in doubt, since the expectant treatment is discouraging.

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A STUDY OF MESENTERIC CYSTS*

WITH A REPORT OF TWO RECENT CASES

By J. Ogle Warfield Jr., M.D.
of Washington, D. C.

In an attempt to bring the subject of mesenteric cysts up to date I have reviewed the literature since 1920 which included 129 case reports. There were probably an additional nine or ten cases, the articles of which were not available. I also submit two successfully operated cases from the records of the Children's Hospital.

History and frequency.—The first case was observed in 1507 by Benevieni, a Florentine anatomist, who accidentally found a mesenteric cyst at autopsy and characterized it as an anatomical curiosity. In 1803 Portal classified these cysts. Rokitansky in 1842 first described a chylous cyst at autopsy. In 1880 Tillaux successfully operated on a cystic mesenteric tumor. Pean in 1883 marsupialized such a tumor successfully and a little later Bramann, Kilian, Millard, and Marklen also treated similar cases surgically. In 1886 Augagneur found that eighteen out of ninety cases of mesenteric tumors were cystic. Arekion in 1891 referred to eighty-one case reports. In 1892 Braquehaye added twenty-three cases, thus making 104. Moynihan in 1897 added nine, and Dowd in 1900 added thirty-two, thus bringing the total published cases to 145. In 1906 Porter estimated the reported cases to be 200. Paskowski in 1912 collected thirty-one cases of dermoid tumors, twelve of which were in the mesentery of the large bowel and rectum, and a year later Mounier collected twenty cases of dermoid cyst of the mesentery. In 1912 Friend collected fifty-two cases of the chylous type and in 1913 Benedict supplemented this and brought the total to ninety-six cases of chylous mesenteric cyst. Carter in 1921 says there have been 200–300 case reports, Higgins and Lloyd in 1924 state about 250, and Flynn in 1930 judges 200–300 cases have been published.

Some writers have divided the history of these tumors into four periods: (1) 1507–1850, when the tumor was observed only at autopsy; (2) 1850–1880, when there was an occasional cyst found at operation, but no recoveries; (3) 1880–1900, when there were some cases of recovery after operation in which the cyst was accidentally found; (4) since 1900, when the condition was suspected and occasionally diagnosed.

Mesenteric tumors are the rarest tumors in the abdomen (Flynn, 1930). Of the true mesenteric tumors the cystic are four times more common than the solid neoplasms. Many text-books barely refer to the subject. A number of physicians of wide experience have neither operated nor seen a case. The majority of writers have been surgeons but a few were pathologists.

* Read before the Medical Society of the District of Columbia, December 16, 1931.

Most authors report a single case but several include two case reports and one author (DePena, 1924) recorded four cases.

It is difficult to estimate the number of reported cases to date. Up to 1900 there were 145 published cases and since 1920 I have reviewed 129 cases. It is fair then to judge that about 500 cases have been reported in the literature.

Etiology and classification.—Portal in 1803 first classified these tumors. In 1842 Rokitansky tried to prove their origin from degenerated lymph nodes. Braquehaye in 1892 classified mesenteric cysts according to their contents and in 1897 Moynihan gave a similar classification and suggested the causes to be (1) hæmorrhage between mesenteric layers; (2) dilatation of lacteals or lymphatics; (3) degeneration of lymph glands. In 1900 Dowd divided these cysts according to their origin into (1) embryonic; (2) hydatid; (3) cystic malignant. He first noted the close embryonic relationship of the wolffian body and the root of the mesentery and suggested that sequestrated cells from the wolffian body might be displaced forward into an intramesenteric position and later develop into a tumor. He also suggested that sequestrated cells from the developing gut might likewise be displaced between the mesentery and develop into a cyst.

Writers since have amplified Dowd's classification and added additional ideas of the genesis of these neoplasms. Each writer has offered a new etiological classification so that to the reader it now becomes confusing. Among these writers I might mention Ayers (1906), Niosi (1907), Gould (1913), Miller (1913), Carter (1921), Bartlett (1923), Higgins and Lloyd (1924), Humiston and Pietti (1925), Hueper (1926), and Wilson (1929).

The causes of mesenteric cysts might be listed as follows:

(1) Embryonic retroperitoneal organs, as germinal epithelium, ovary, wolffian or müllerian bodies. Remnants of these organs become displaced forward between the mesenteric layers. Many of these neoplasms develop in this manner. The rare pararenal cysts probably originate from wolffian body remnants but retain their position and are not displaced into the mesentery. These cysts bear a close resemblance to the mesenteric cysts. Dermoids of the mesentery apparently arise from the ovary. No retroperitoneal nor mesenteric dermoids have been reported in the male though they have occurred in the testis (Ayers, 1906) which is originally a retroperitoneal organ. Swartley (1927) reports a sebaceous cyst in a male, twenty-six years, and Forster (1921) an epidermoid in a male, fourteen years. Both of these occurred in the jejunal mesentery but neither seems to have been a true dermoid so the fact that mesenteric dermoids always occur in the female and arise from the ovary still holds.

(2) Displaced embryonal intestinal tissue. Sequestrations from intestinal diverticula or from the vitelline duct become displaced between the mesenteric layers. In 1908 Lewis and Thyng described the regular occurrence of intestinal diverticula in embryos of the pig, rabbit and man and established the fact that the formation of diverticula and cysts is a regular occurrence

in the embryonic development of the gut. Hence cysts from intestinal diverticula may occur anywhere along the bowel while those from the vitelline duct occur principally in the terminal ileum. Like the first cause many of these tumors also develop in this manner.

(3) Dermal inclusions. This origin was suggested by Bartlett (1923) but probably very few if any arise from dermal inclusions.

(4) Angiomas of blood and lymph vessels. This also includes but few of these cysts.

(5) Parasitic and bacterial infection. A few mesenteric cysts have originated from the echinococcus and from tuberculous abscesses.

(6) Necrosis of lymph glands or solid tumors, as tuberculosis, typhoid fever, lipomata, malignant tumors, *etc.*, is responsible for a few of these cysts.

(7) Trauma and foreign bodies. Hæmatoma from injury may degenerate to form a cyst. Usher (1926) reports such a case. Genkin (1928) removed a chylous cyst formed around a gauze tampon left in at a previous operation.

(8) Lymphatic obstruction. This possible origin of mesenteric cysts has practically been discarded. These lymphatic vessels anastomose so freely it is hardly conceivable that plugging of a chylous vessel would produce a cyst.

Cases are recorded at all ages from the fœtus to the octogenarian but the fourth decade is most common. Women are affected twice as often as men. Very few are reported in the colored race.

Age	Cases	Sex	Cases
0–1	9		
1–10	21	Female	71
10–20	16		
20–30	18	Male	37
30–40	24		
40–50	17		
50–60	11	Unknown	21
60–70	3		
unknown	10		

Symptomatology and diagnosis.—There are no pathognomonic signs nor symptoms. The tumor is often too large or too small to accurately diagnose. Contrary to previous writers mesenteric cysts have been diagnosed before operation in a few cases, certainly since 1920 and probably before. Reports recording correct diagnoses are Haworth (1920), Bertolini (1921), Naumann (1921), Levinson and Wolfsohn (1926), Ciarlo (1927), Aloi (1927), and Finucci (1930). Others have suspected the condition.

An abdominal tumor which is rounded, smooth, not tender, cystic and quite mobile should suggest the probability of a mesenteric cyst. The mobility of the tumor is often striking and especially in the transverse direction,

due to its mesenteric attachment. Pain is more frequently present than with any other type of abdominal cystic tumor.

Other symptoms are due to the presence of some complication, principally intestinal obstruction. Hence a story of repeated attacks of abdominal pain sometimes with vomiting and alternating periods of diarrhœa and constipation is very important. The patient's weight may increase or decrease.

To repeat then, the symptoms may be those of a silent, cystic, abdominal tumor or those of intestinal obstruction. In the presence of rupture of the cyst or acute inflammation it is difficult to differentiate this condition from the other causes of an acute surgical abdomen. Hancock (1929), however, reports that he found at operation a ruptured cyst of the transverse mesocolon which had produced no acute symptoms.

Viadya (1927) reported a cyst of the ascending mesocolon which he only aspirated at operation and which filled again, and three weeks after the operation it apparently ruptured into the bowel for the patient passed quantities of liquid similar to the contents of the tumor and the distended abdomen became flattened.

In the differential diagnosis other conditions which must be considered are ovarian cyst, retroperitoneal tumors, pancreatic cysts, intestinal new-growths, pedunculated uterine fibroids, movable kidney, hydronephrosis, hydrops of the gall-bladder, ascites, tuberculous peritonitis, pregnancy, acute appendicitis, cholycystitis, intestinal obstruction, intussusception, perforated peptic ulcer, extrauterine pregnancy, ruptured pelvic or tubal abscess, acute peritonitis, acute pancreatitis, and acute diverticulitis.

To differentiate between the types of mesenteric cyst is practically impossible except on pathological examination.

Location.—Mesenteric cysts may occur anywhere along the intestinal tract from the duodenum to the rectum. Over half of the cases occur in the small bowel and one-fourth in the mesentery of the ileum. Of those in the large bowel the ascending, transverse and sigmoid colons share about equally.

Of the 129 cases reviewed I have listed the location of the cyst in order of frequency as follows:

Ileum	38	Appendix	2
Jejunum	14	Duodenum	1
Cæcum and ascending colon	14	Gastro-hepatic mesentery	1
Transverse colon	13	Colon (portion unknown)	6
Sigmoid	12	Small bowel (portion unknown)	6
Descending colon	5	Unknown	15
Duodeno-jejunal juncture	2		

Pathology.—These neoplasms may be so small that they cannot be palpated or so large that they practically fill the entire abdomen. The greater majority are single cysts, though a few are recorded of multiple tumors. About one-half of the cases are unilocular while the other half present two or more compartments. A duct connecting two cysts or a cyst and the intestinal lumen is said to have been described. (Hueper, 1926.)

The cyst wall is usually thin but varies in thickness and composition. The lining of these tumors is mostly epithelial though often destroyed by the internal pressure of the cyst. The epithelium is usually simple columnar, sometimes stratified and rarely ciliated. The structure of the cyst wall very often reveals the genesis of the neoplasm. The presence of primitive glomeruli demonstrate wolffian-body origin. Layers of smooth muscle, epithelium, and sometimes goblet cells establish intestinal tract etiology. An endothelial lining suggests the tumor arose from a lymphangioma. High columnar epithelium and pseudomucin or the presence of hair, teeth, *etc.*, indicate primitive sex-organ ancestry.

The contents of these tumors denote accidents that have befallen the cyst and only occasionally have any bearing on the etiology. The first classifications were based upon the cystic contents and included such terms as serous, lymphatic, lymphorrhagic, chylous, sanguinous and hæmorrhagic. The lymphatic and chylous cysts are about equally divided in number. The fluid may be clear, colorless, yellow, milky, mucinous, brown, sebaceous, or bloody. The reaction is alkaline, the specific gravity about 1.015 or 1.016. It often contains a large amount of albumin, cell débris, blood and cholestrin.

Malignant degeneration is rare and may be either carcinoma or sarcoma.

The case reports since 1920 might be classified pathologically as lymphatic or serous thirty, chylous twenty-eight, hæmorrhagic nine, dermoid six, malignant three, (one adenocarcinoma and two spindle-cell sarcoma), sebaceous two, epidermoid one, echinococcal one, unknown forty-nine.

Complications.—(1) Intestinal obstruction is the most frequent and most serious of the complications. It occurs in one-third of the cases and of these the mortality is 50 per cent. The obstruction is mechanical and includes intestinal narrowing or occlusion, kinking, volvulus, adhesions, and intussusception. Sala and Nachamie (1929) reported a case of prenatal volvulus of both the small and undescended large bowel and mention that two cases of prenatal volvulus of the small intestine had been reported in the past fifteen years.

Other complications occur only occasionally.

(2) Peritonitis is a sequel to obstruction.

(3) Hæmorrhage into the cyst has been fatal.

(4) Rupture of the cyst into the peritoneum or into the bowel has caused death. This may occur spontaneously or be due to trauma.

(5) Torsion of the cyst.

(6) Impaction of the cyst in the pelvis causes symptoms depending on the organ upon which it presses.

Ordinary post-operative complications sometimes occur such as shock, pneumonia, dilatation of the stomach, post-operative hernia, recurrence of the cyst after incomplete removal, *etc.*

Prognosis.—The prognosis depends upon the size, location, site of attachments, time of diagnosis and operation, whether benign or malignant,

type of operation, presence of complications, age and general condition of the patient.

Treatment.—The treatment of mesenteric cyst is entirely surgical. In the acute cases the treatment is directed principally toward the complications, the chief one being intestinal obstruction, while in the subacute and chronic cases the operation consists of removing or obliterating the mesentric cyst by one of several methods.

(1) Enucleation is undoubtedly the operation of choice, but it is not always feasible without injuring the bowel and hence each case must be studied at operation to determine the technic best adapted to the case at hand. This procedure is the one most often used and with the lowest mortality—9 per cent.

(2) Enucleation with intestinal resection is often necessary and has a mortality of 27.3 per cent. The enterogenous tumors usually cannot be separated from the intestine and require resection.

(3) Either drainage or marsupialization has been done in a number of cases and certainly has a place in the treatment of large, extensively adherent mesenteric cysts where enucleation even with resection is out of the question. The mortality of these two procedures in the reviewed series of cases was 16.6 per cent. This seems high and includes deaths due to complications. The mortality rate is better judged perhaps by the kind of complications present, size and location of the tumors, *etc.*, than by the type of operation employed. Marsupialization or drainage is rarely apt to result in a permanent sinus or recurrence which would ultimately require excision. The length of time of drainage varies from one to three months. Gurewic (1926) reports a cured case after marsupialization of a chylous cyst of the mesosigmoid that drained for one year. There have been several recurrences following drainage that afterwards have been enucleated.

(4) Aspiration may at times be helpful in diagnosis but should not be employed in the treatment of these tumors. It was often used by the older surgeons and there is an occasional case of recent years that has been aspirated.

The following table gives the types of operation used and results of the cases reported since 1920.

Operation	Cases	Cured	Recovered	Died	Res. Unknown
Enucleation	56	42	..	5	9
Enucleation with resection	22	14	..	6	2
Marsupialization	15	11	..	1	3
Drainage	5	2	..	3	..
Aspiration	4	..	3	1	..
Laparotomy	24	8	2	5	9
Autopsy	3	..	..	3	..

Of the twenty-four deaths the diagnosis before operation was obstruction in twelve, abdominal tumor in five, peritonitis in two, appendicitis in one, ectoptic pregnancy in one, gall-bladder disease in one and unknown in two.

The location of these cysts was jejunum eight, colon seven, (transverse four), ileum seven, duodenum one, and unknown one. Thirteen of the twenty-four deaths were in cases of five years or under, six were over thirty years and five between five and thirty years of age. The deaths were equally divided in sex.

CASE I.—White, male, six years, admitted to Children's Hospital, September 20, 1930.

History.—Swelling of the abdomen for three weeks. Appetite good, no constipation, vomiting, fever, night sweats nor urinary symptoms except enuresis. He was a full-term baby and breast fed for nine months. The only illnesses have been colds and at six months of age a diarrhœa which lasted several weeks. Both parents living and well. Three other children well. No tuberculosis in the family.

Examination.—Temperature 99.2°, pulse 100, respiration 26. Weight 42 pounds. The child was anæmic looking, thin, and with a greatly distended abdomen. Teeth in poor condition and tonsils enlarged. Heart and lungs negative. There was some chronic adenitis of cervical, axillary and inguinal nodes. The abdomen was symmetrically distended, tense, flat on percussion, cystic, with a flare at the costal margins and the skin stretched. No abdominal organs could be palpated and no tenderness, tumor mass nor rigidity was noted. Extremities negative. The blood on admission showed red blood cells 3,180,000, hæmoglobin 63 per cent., white blood cells, 6,700, lymphocytes 51 per cent., polymorphonuclears 49 per cent. (lobulated 45, bands 4). The urine was repeatedly negative. The Wassermann was negative (October 6). Röntgen studies revealed the heart enlarged to the left, thymus 34 per cent. Both diaphragms were displaced upward and the abdominal walls flared out; probably fluid in the abdominal cavity. The colon was negative. Several tuberculin tests were negative. Laryngoscopic examination showed hoarseness and redness of the vocal cords suggestive of tuberculosis. No tubercles were seen and smears were negative for the tubercle bacillus.

The impression was tubercular peritonitis and laryngitis, and diet, rest and ultraviolet therapy were advised. The child showed no progress. His weight increased 1 pound (43) but the abdomen became more distended; the blood-picture and hoarseness remained the same. The abdomen was tapped November 1, and November 25, 1930. Each time 20 cubic centimetres of bloody fluid was withdrawn, showing no growth on culture nor tubercle bacilli on smears. A laparotomy was finally decided upon.

Operation.—(By author) November 28, 1930. Avertin anæsthesia. A low mid-line incision revealed no free fluid. There presented a very large, dark-bluish, cystic tumor attached along the entire left lateral peritoneal wall, across the brim of the pelvis, bulging into the mesentery of the ascending and transverse colons and extending high up toward the liver and spleen where it was attached to the posterior peritoneum. It seemed to have two large cystic lobules, one toward the liver, and the other toward the upper left quadrant. The ascending and most of the transverse colon were seen to the right of and running across the upper portion of the tumor toward the left. The cæcum was fixed in the pelvis at or beneath the attachment of the cyst and was not seen. The small intestine was felt in the upper right quadrant and also seen after the cyst was opened. The ascending and transverse colon and small bowel were of normal appearance. The cyst was opened in the mid-line and contained bloody fluid. The cyst wall was thin and its lining smooth and shiny. This emptied only one lobule and a large lobule on the right was opened from the mesial side and underneath the ascending colon. There was possibly another lobule high up posteriorly that could not be reached but it was hoped this might communicate with the compartments already opened. The cyst wall was sutured to the anterior parietes and a rubber tube drain was placed in each lobule. About 1,900 cubic centimetres of bloody fluid was aspirated and approximately an equal amount spilled on the floor. Closure.

Laboratory Examination of the fluid revealed 1,900 cells per cubic millimetre. No pancreatic enzymes were present.

The temperature came down in a few days and the drainage was profuse. On the ninth post-operative day (December 7th), the temperature rose to 103° and became septic. The white blood cells varied from 18,000 to 20,000 with 85 per cent. to 90 per cent. polymorphonuclears and 18 to 25 band forms. The drainage changed to seropurulent and lessened. On palpation a large, tender mass appeared in the right side of the abdomen.

Second Operation.—December 24, 1930. Avertin anæsthesia. The sinus was explored with the finger and found to run up, back and to the left. The lobule on the right had closed but was opened and emptied of a large amount of foul, brown fluid. Six rubber drainage tubes were inserted.

His convalescence was long. The drainage was yellowish brown. The temperature slowly lowered but lasted for five weeks. The drainage tubes were very gradually shortened and removed six weeks after the second operation. Ultraviolet therapy helped considerably. His lowest weight was 32 pounds and on discharge (February 17, 1931) 41½ pounds.

On March 9, 1931, his weight was 45 pounds, red blood cells 4,600,000, white blood cells 8,000, hæmoglobin 75 per cent. The wound had healed and the abdomen was flat, symmetrical, soft, not tender, and there was no palpable mass. The hoarseness had improved.

Five months after operation (June 8, 1931) the boy looked well but pale. He played hard, had gained weight, ate well and the bowels were regular. The abdomen was flat without masses, tenderness or rigidity. The operative scar had widened and there was a separation of the recti muscles between which intestines protruded on straining.

He was seen November 11, 1931, about one year since operation. He is slender and pale but has been well and attending school. The recti muscles are separated ¾ inch below the umbilicus. Otherwise the abdomen is negative.

CASE II.—White, male, two and one-half years, admitted to Children's Hospital September 16, 1929. There were no symptoms. An abdominal tumor had been noticed at a baby show. Examination revealed a movable, cystic mass the size of a small grapefruit in the lower abdomen. The pediatrician (Doctor Copeland) made a diagnosis of mesenteric cyst. At operation (Doctor White) a serous cyst containing yellow fluid was enucleated from the mesentery of the small bowel. The convalescence was smooth and the child left the hospital in twelve days.

Summary.—The first case was observed at autopsy by Benevieni in 1507. Tillaux in 1880 successfully operated on a cystic mesenteric tumor. There have been approximately 500 cases reported to date. Dowd in 1900 classified these neoplasms according to their origin, which is chiefly embryonic from mesodermal remnants behind the developing peritoneum of from intestinal diverticula or persistent portions of the vitelline duct. There are no pathognomonic signs nor symptoms. One-half of these tumors occur in the small intestine and one-fourth in the mesentery of the ileum. The structure of the cyst wall varies with the origin of the tumor, while its contents have little bearing on the etiology. One-third of these cysts are complicated by intestinal obstruction in which the mortality is 50 per cent. The treatment consists of enucleation with or without intestinal resection, drainage, or marsupialization.

The two cases reported contrast the difficulty and simplicity of treat-

ment. The first case reported illustrates the fact that the tumor was too large to diagnose correctly though the fluid removed at several tappings should have been more completely examined. The operation of choice was certainly marsupialization due to the enormous size and extensive attachments of a multilocular cyst. I believe the tumor originated in the mesentery of the ascending colon. Unfortunately, a pathological section was not obtained and hence the etiology is not known. It was no doubt embryonic and possibly pressure from the growth had destroyed any definite pathology of the cyst wall. A second operation was necessary to establish adequate drainage which lasted for two and one-half months. The child was seen nearly one year after the operation and had a diastasis of the recti muscles but there was no evidence of a recurrence of the cyst.

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MESENTERIC AND OMENTAL CYSTS*

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It is the purpose of this paper to report five cases of mesenteric and one case of omental cyst, operated upon without mortality; to record a correct pre-operative diagnosis; and to offer a suggestion as to a method of surgical treatment, in selected instances, which, so far as I am aware, has not hitherto been proposed.

Since 1507, when Benevieni, a Florentine anatomist, found at autopsy and recorded it as an anatomical marvel, there have been published between 250 and 300 cases of mesenteric cysts. In 1852, Gairdner reported before the Pathological Society of London an autopsy specimen of an omental cyst, since which time there have been published slightly over fifty cases. The ratio of mesenteric to omental cysts is about 5 to 1. The two conditions are considered similar in origin and histological structure.

The theories of the older pathologists regarding the genesis of mesenteric cysts were clouded in obscurity and uncertainty. Such cysts were thought to result from "lymph stasis and from cystic degeneration of a lipoma or of tuberculous glands." Dowd's paper,[1] in 1900, was notable for its clearness and originality, and for the renewed interest in this subject which its publication aroused. He stated his belief that such cysts developed from embryonic remnants and sequestrated intestinal tissue and he suggested that they be classified as (1) embryonic; (2) hydatid; and (3) cystic malignant disease.

Niosi,[2] in 1907, expressed the opinion that about one-half of all mesenteric cysts are acquired, and he placed the so-called lymphatic and chylous types in this category. He classified embryonic mesenteric cysts as:

(1) Cysts of intestinal origin:
  (*a*) By sequestration from the bowel during development.
  (*b*) From Meckel's diverticulum, when it arises from the concave side of the bowel or (as Miller has added) acquires an intramesenteric position.
(2) Dermoid cysts.
(3) Cysts arising from retroperitoneal organs, *viz.*—urogenital organs (germinal epithelium, ovary, Wolffian body or Mullerian duct).

Eric Gould,[3] in 1913, believed the following to be simplest and most correct pathological classification:

(1) Cysts arising from embryonic remnants and sequestrated tissue: (*a*) serous; (*b*) chylous; (*c*) sanguineous; (*d*) dermoids; (*e*) cysts from intestinal diverticula.

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(2) Cysts of infective origin: (*a*) hydatids and (*b*) tuberculous abscesses.
(3) Malignant cysts.

Higgins and Lloyd,[4] in 1924, say that "such adjectives as lymphatic, chylous, sanguineous, though frequently used, merely denote accidents which may befall any cyst, and, though picturesque, they have no precise bearing on the problems of etiology and serve no useful purpose." Out of the mass of material studied, and the classifications reviewed, they offer these conclusions:

(1) True mesenteric cysts are not malignant, parasitic or dermoid, but form a separate group in which are included the majority of all "mesenteric cysts."
(2) Their origin is still in doubt, but it seems probable that there are two classes:
  (*a*) Cysts of embryonic origin arising from mesodermal remnants incarcerated behind the developing peritoneum and subsequently migrating forward between its layers.
  (*b*) Cysts of intestinal origin: (1) Arising in most cases as diverticula from the bowel during development; (2) possibly derived sometimes from persistent portions of the vitelline duct.
(3) Anomalous and hitherto unclassified cysts, such as pararenal.

Mesenteric cysts occur somewhat more frequently in the female than in the male sex. They have been found at all ages—in the fœtus and in an octogenarian. They may be single or multiple, unilocular or multilocular, and may vary in size from that of an olive to enormous growths filling the abdominal cavity. The original histological picture may be so altered from hæmorrhage, pressure, inflammation or malignant degeneration that it is difficult for the pathologist to render a satisfactory report as to the origin and structure of the cyst.

Case Reports.—Case I.—J. M., male, aged five years and ten months, of Italian parentage, was admitted to the Post-Graduate Hospital December 26, 1917, with a history of generalized abdominal pain, which had localized in the right lower quadrant, accompanied by nausea, vomiting and obstinate constipation.

Two years ago it was noticed that the boy's abdomen was growing larger and an exploratory operation a year later revealed a tuberculous peritonitis. The abdominal cavity was flushed out with full strength hydrogen peroxide and closed without drainage. It could not be learned from the history just what type of tuberculous peritonitis was found.

Physical examination was negative except for muscular spasm, resistance, and marked tenderness in right lower abdominal quadrant, and the presence of a very tender tumor mass. A diagnosis of acute appendicitis with abscess was made, and the patient was sent at once to the operating room.

On opening the abdomen the appendix was delivered, but failed to show any active inflammation. However, in the mesentery of the lower ileum, near the ileocolic angle, a cystic tumor, yellow in color, about eight by four by four centimetres in size, was found. Enucleation of the cyst could not be wholly accomplished, without sacrificing a relatively large blood-vessel, which was feared would result in gangrene of a small area of intestine. Rather than do a bowel resection, a small segment of the cyst wall, containing the blood-vessel, was left behind, the major portion of the cyst being removed. Carbolic acid followed by alcohol were applied to the remaining cyst membrane, which was then brought up to the abdominal incision, and the wound was closed in layers, except at a point where a narrow strip of iodoform gauze went down to the segment of the cyst wall left behind. Healing was prompt and without sinus formation or recurrence of the cyst. Patient was discharged two and one-half weeks after opera-

tion. An interesting observation at the time was the fact that there was absolutely no other evidence of the tuberculous peritonitis which had been found at operation a year before.

Pathological report (Dr. L. H. Meeker).—*Gross.*—Specimen is an opened sac, the size of a lemon. The surface is hæmorrhagic and at one side are thickened reduplications of peritoneum. The wall varies in thickness from ½ millimetre to ⅞ millimetre, is fibrous, and clinging to the inner side is caseous white granular material. At one point, beneath the entangled peritoneum, are small packets of this material. The wall is tough fibrous tissue.

Microscopical.—Under a capsule of dense fibrous tissue is an admixture of semi-necrotic areas of fibroblastic and epithelioid cells, coalescing and frequently showing giant cells of the foreign-body type. All this tissue is invaded by round cells and surrounds a caseous core. No normal grand tissue remains.

Diagnosis.—Probably cystic degeneration of a tuberculous lymph-node.

Case II.—C. P., a woman, aged thirty-one years, married for fifteen years, but never pregnant, was admitted to the Post-Graduate Hospital, June 24, 1918, complaining of great weakness and fatigue, backache, abdominal discomfort, constipation, *etc.* Only three weeks before had she become aware of the presence of a large tumor in her lower abdomen. Although menstruation had been regular previously, for over a year there had been no menstrual flow. There was no appreciable loss of weight, in spite of two weeks' confinement to bed and a restricted diet.

Physical examination showed nothing of importance except a large, tense, symmetrical tumor in the lower abdomen, apparently rising out of the pelvis. The tumor did not move with respiration, was flat on percussion, and showed no pulsation. No fœtal heart sounds could be heard. Vaginal examination showed the cervix crowded down to the vaginal introitus; the body of the uterus could not be mapped out. Rectal examination was negative, except for the presence of the large cystic tumor. *Diagnosis.*—Ovarian cyst.

When the abdomen was opened a large cyst was seen, with evidences of both old and recent active peritonitis. The coils of intestine were so adherent to the cyst that it could not be delivered or shelled out of its mesenteric bed. There was no connection whatever with the ovaries. The cyst was opened and a large quantity, probably over a gallon, of dark, straw-colored, serous fluid was evacuated. A section of the cyst was removed for histological study, then marsupialization and packing of the cyst cavity with washed-out iodoform gauze completed the operation. The first ten post-operative days were rather stormy. The profuse serosanguineous discharge necessitated frequent changes of dressing. The discharge rapidly lessened and the patient returned to her home three and one-half weeks after operation. The sinus was entirely healed at the end of three months, and the patient has remained well, without any abdominal complications since.

Pathological report (Dr. L. H. Meeker).—*Gross.*—Specimen is a portion of a cyst wall roughly seven by two centimetres. One side is fairly smooth and the other is granular and hæmorrhagic. One wall is several millimetres thick and is very tough.

Microscopical.—The cyst wall is composed of layers of fibrin with few fibroblasts and scattered blood-vessels, and some round cells. One-half its thickness presents a classical picture of foreign-body giant cells which have ingested cholesterin crystals. It would seem that adhesions have created a cyst the contents of which included cholesterol. *Diagnosis.*—Simple cyst within adhesions.

Case III.—S. C., male, aged six years, of healthy Italian parentage, was admitted to the Babies' Wards, Post-Graduate Hospital, April 28, 1927. At fifteen months of age the boy had had, in the order named, measles, whooping-cough, pneumonia and multiple furuncles, from which he made a good recovery. At four years of age, it was noticed that his abdomen was somewhat larger than normal, but otherwise he seemed perfectly well. Three weeks before admission there developed an acute attack of ab-

dominal pain, with high fever, vomiting and constipation, but the attack subsided after three or four days. No definite diagnosis was made at this time. Upon admission, the examination revealed an irregular enlargement of the abdomen and an acute right-sided epididymitis. A large, movable, nodular, tense, cystic mass, occupying the right side of the abdomen and extending over beyond the median line, could be felt. In the left upper abdomen there was distended tympanitic bowel.

May 6, 1927, the abdomen was opened and the tumor mass was found to be a large cyst and two smaller cysts of the mesentery, grouped together and intimately connected with the lower ileum. It could be lifted out of the abdomen easily. An attempt was made to enucleate the cysts from the mesentery but it was found impossible of accomplishment, without sacrificing the blood supply to the bowel. It was necessary to resect about eight inches of intestine in order to remove the tumors. An end-to-end suture anastomosis of the ileum was performed without difficulty. The patient made a prompt and uninterrupted recovery and was able to leave the hospital two weeks after operation.

Pathological report (Ward J. MacNeal, M.D.).—*Gross.*—Specimen measured 160 by 115 by 80 millimetres. It included a portion of intestine, apparently the small intestine, 110 millimetres long and ten to twenty-two millimetres in diameter. Intimately attached at one side of this piece of gut there were three cysts; one was sixty millimetres, another thirty-five millimetres, and the other 120 millimetres in diameter. These were opened. The wall of the cysts in each case was about one and one-half millimetres thick.

Microscopical.—Sections through the wall of the intestine including the wall of one of the adjacent cysts showed moderate inflammatory reaction in the mucous membrane of the gut and some thickening of the muscular coats. The cyst was lined by granulation tissue in which there were abundant clefts from which lipoid material had been dissolved out. In this granulation tissue there were abundant multinucleated giant cells of the foreign-body type. The superficial portion of the lining was necrotic. It was impossible to recognize any elements of intestinal mucous membrane in the lining of the cyst in these sections. *Diagnosis.*—Multiple cysts of the mesentery intimately attached to the small intestine, of unrecognized origin.

Dr. Nicholas M. Alter later examined the specimen and reported as follows: "The description by Doctor MacNeal fits the microscopical picture accurately. I do not think the cyst is of intestinal origin or derived from the omphaloenteric duct. I think it should fall in Gould's classification (Group I), of embryonic cysts of chylous origin. In the lower layer of the cyst wall there are very numerous dilated lymph-vessels and chylous cells are seen in many of these dilations."

Case IV.—S. S., a man, aged fifty-nine years, born in Russia, was admitted to the Post-Graduate Hospital, October 15, 1929, complaining of gradual loss of weight (15 pounds) and strength, increasing constipation with subacute attacks of intestinal obstruction. Appetite poor, digestion fair, some nausea, but no actual vomiting. No blood or pus in stools. Symptoms began about six months ago. After an X-ray study of the gastro-intestinal tract, in a Brooklyn Hospital, a diagnosis was made of "carcinoma of the ascending colon."

The general physical examination revealed nothing of importance. Abdominal examination showed considerable tumefaction on the right side, about opposite the umbilicus, and the diagnosis of carcinoma of the colon seemed probable.

Upon opening the abdomen a large, hard mass was at once encountered, but it involved the ileum and not the large intestine. Coils of ileum were adherent about this tumor, which was thought to be a new growth in the ileum, with extensive metastasis in the mesentery. The involved bowel and mesentery were widely resected, followed by an end-to-end suture anastomosis. The patient stood the operation well, but his convalescence was unusually stormy and exciting. He finally made a good recovery, except for an incisional hernia.

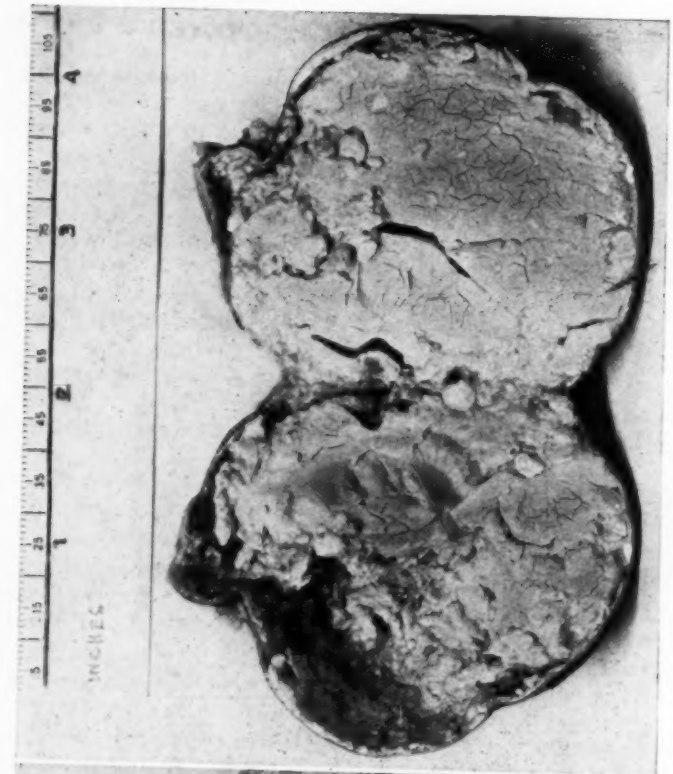

FIG. 2.—Case V. Mesenteric cyst filled with thick sebaceous material. Two smaller cysts had similar contents.

FIG. 1.—Case III. Multiple cysts of the mesentery. Note narrowing of intestine from pressure.

Pathological report (Dr. Nicholas M. Alter).—*Gross.*—Specimen consists of a large portion of the small intestine with mesentery attached. It measures 280 centimetres (about nine and one-half feet) in length. The loops of the small intestine are moderately distended and are firmly adherent to a central mass which seems to come up from near the ileum about fifteen centimetres from the surgical stump of the ileum and from this extends into the mesentery which is adherent to the other loops of the intestine. This mass is very hard in consistency and measures about ten centimetres in diameter. On opening no obstruction is encountered. The lumen of the ileum is free. From the ileum a cystic cavity is opening which has an orifice six centimetres in diameter. This leads into a somewhat larger cavity which contains a great deal of greenish vegetable matter, a large amount of mucus and broken-down necrotic material and the wall is covered with a polypoid growth which is very hard at the base and on section shows gray translucent appearance. The growth is very hard, cartilaginous almost.

Microscopical.—Section of the growth shows neoplastic proliferation of small polygonal cells with large vesicular nuclei. The cells are quite anaplastic, show great variety of size and shape and form a rather diffuse growth. There is a suggestion only here and there of glandular structures and there is a vascular stroma. The growth ulcerates over the mucosa and infiltrates the muscle layer but has a rather sharp border.

Diagnosis.—Embryonal carcinoma of mesenteric cyst.

January 14, 1932, two and one-quarter years after the operation already described, the patient was operated upon for the repair of the incisional hernia. Upon exploration of the abdomen the exact site of the anastomosis could not be determined, so perfect was the union, and it is gratifying to report that there was absolutely no evidence of recurrence of the malignant disease.

Case V.—Mrs. E. G., twenty-six years of age, was seen in consultation with Dr. A. A. Weiss, of this city, April 10, 1930. Three or four days before she had complained of abdominal pain, which had localized in the right lower abdomen. The pain was not severe, but as it persisted, the family physician was called. There was some nausea, but no vomiting. Bowels, usually regular, were constipated. There was only slight elevation of temperature, the urine was negative, and a blood examination showed some increase in the total leucocytes and the percentage of polymorphonuclear cells. The patient has always considered herself an exceptionally healthy individual.

The physical examination was negative except for rather marked tenderness over McBurney's point, with some muscular spasm and resistance. In the course of the examination, however, a rounded, freely movable, non-tender tumor was discovered, just to the right of and below the umbilicus. When questioned about it the patient said that she had known of its presence since she was sixteen years of age, but as it had never caused her any inconvenience whatever, it gave her no concern. She entered Post-Graduate Hospital that night and was operated upon early the following morning.

The abdomen was entered through a pararectus (Kammerer) incision. The appendix was readily delivered and removed. The ileum was then pulled up and a tumor mass consisting of three mesenteric cysts in the lower ileum was delivered. These cysts were carefully enucleated from the mesentery, without any damage to the blood supply of the bowel. The openings in the mesentery were closed with plain catgut sutures. The immediate clinical diagnosis was recorded as "subacute appendicitis" and "dermoid cysts (3) of the mesentery." One of the cysts was opened during its removal and was filled with thick sebaceous material. Although no hair or bone was discovered the contents of the cyst looked typical of the usual material found in dermoid cysts.

Following operation the patient suffered considerable nausea, vomiting, and abdominal discomfort for two or three days, after which time she made an unusually smooth convalescence, and was able to leave the hospital on the ninth post-operative day. Her health has been perfect since the operation.

Pathological report (Dr. W. J. MacNeal).—*Gross.*—Appendix is fifty-six millimetres long and seven to eight millimetres in diameter. On section the lumen extends to the

tip. In it there is one very firm lump ten by four by three millimetres, dark brown in color, apparently a fecolith.

Second specimen appears to have been a cyst about thirty millimetres in diameter with a wall one to two millimetres in thickness, rather firm. The material in the interior is in part soft cheesy stuff and in part is calcified.

Third specimen is a cyst seventy-two by sixty by forty-six millimetres. This is said by Doctor Peterson to resemble the cyst which has been broken open and this second cyst is left intact by his request.

Microscopical.—Sections of the appendix show partial loss of lining mucous membrane with purulent exudate extending into the submucous layer in the regions of ulceration. The muscular coats and the subserous coat are very œdematous and richly infiltrated by lymphocytes and plasma cells with smaller numbers of polymorphonuclear leucocytes intermingled.

Sections of the wall of the opened cyst show a lining of necrotic material beneath which there is a zone of epithelioid cells containing occasional poorly defined multinucleated giant cells and intermingled with lymphocytes. External to this there is a layer of fibrous tissue containing abundant lymphocytes and at one place a small nodule of epithelioid cells suggesting a small tubercle.

Diagnosis.—(1) Acute purulent exacerbation of a chronic appendicitis; subacute peri-appendicitis. (2) The diagnosis is somewhat uncertain, as tubercle bacilli have not been demonstrated in the cyst. However, the diagnosis of tuberculosis seems most probable.

Omental Cyst.—Case I.—J. B., aged four years, admitted to Post-Graduate Hospital, February 27, 1921, complaining of abdominal pain and fever, but no vomiting. Bowels had moved normally the day before. Patient looked sick. Lips covered with fever blisters. Had previously had measles and chicken-pox. When fourteen months old had been operated upon for mastoid trouble.

Physical examination negative except for slight distension, marked tenderness and board-like rigidity over the whole lower abdomen. It was not possible to make a satisfactory examination without giving an anæsthetic. *Impression.*—Acute appendicitis with peritonitis. Patient sent at once to operating room for emergency operation. Upon entering the abdomen a cystic tumor mass, in the large omentum, was recognized at once. The appendix showed no gross pathology, but was removed as a prophylactic measure. The cyst-bearing omentum was resected with ease. The patient made a prompt and uninterrupted recovery.

Pathological report (Dr. Nicholas M. Alter).—*Gross.*—Specimen consists of a cystic mass with some fatty tissue attached, evidently portion of the omentum. The mass is lobulated, cystic, well encapsulated. Some of the cysts are evidently leaking clear serous fluid. The mass measures about 11 by eight by four centimetres. On section multilocular cavities are seen filled with yellowish jelly-like material and some white membranes. Otherwise the cysts seem to have smooth but congested lining. The wall of the cyst averages two to three millimetres and is fibrotic. The outer surface is covered with fibrous and fatty tags.

Microscopical.—Section shows some endothelial lining of the cyst. The endothelial cells are quite hyperplastic in many places. The surface is covered with some mucoid fibrinous material which contains a great many polymorphonuclear leucocytes. These polymorphonuclear leucocytes also infiltrate the entire wall which otherwise consists of loose fibrous structure.

Diagnosis.—Congenital peritoneal cyst of omentum with acute secondary infection.

Comment.—Omental cysts are similar in origin and structure to mesenteric cysts. The surgical treatment is, as a rule, a very simple matter and the mortality in the reported cases said to be about 6 per cent. The symptoms in my case were caused by inflammation of the cysts and local peritonitis.

SUMMARY.—*Symptoms and diagnosis.*—In the first case the symptoms were typical of acute appendicitis, *viz.*, abdominal pain, general in character at first, later localizing in the right lower quadrant, nausea, vomiting and constipation, with muscular rigidity and spasm and marked localized tenderness. Pre-operative diagnosis—acute appendicitis with abscess; post-operative and pathological diagnosis—cystic degeneration of a tuberculous lymph-node.

In the second case the symptoms of weakness and fatigue, backache, abdominal pain, constipation, and the downward displacement of the uterus, were caused by peritonitis and pressure. The preliminary diagnosis of ovarian cyst was incorrect. The pathological diagnosis of simple cyst due to foreign body (?), or gauze sponge from previous operation (?) is incorrect too, for the patient had undergone no previous operation. This is believed to be one of the rare, intraperitoneal cysts, of *nephrogenic* origin, in Group III, of Ewing's classification.* These cysts occur chiefly in adult women, are of large size, single or multilocular, involve the mesentery or adjacent regions or extend into the pelvis. The contents are brownish, serous fluid, containing pseudomucin.

In the third case the symptoms were of chronic intestinal obstruction, due to pressure-narrowing of the bowel by the cysts. (Intestinal obstruction, either acute or chronic, is the most important and frequent complication of mesenteric cysts. It may be from volvulus, intussusception, kinking and pressure-narrowing or occlusion of the adjacent intestine. Other complications are (1) hæmorrhage into the cyst, (2) torsion of the cyst, and (3) rupture of the cyst. In this case the diagnosis should have been made. Practically everything but mesenteric cyst was considered and it was not even thought of. The pathological diagnosis was embryonic mesenteric cyst of the chylous type.

In the fourth case the symptoms were of chronic intestinal obstruction, with subacute exacerbations. The preliminary diagnosis of a malignant growth of the intestine, causing obstructive symptoms, was again wrong. The pathological diagnosis of "carcinoma of an embryonal mesenteric cyst" places the case in a most remarkable and unusual class. Cystic malignant disease of the mesentery is not uncommon, but malignancy developing in an embryonic mesenteric cyst is both interesting and rare. Doctor Alter's microscopical report stating "the growth ulcerates over the mucosa and infiltrates the muscle layer" and the further observation that there was an opening from the ileum into the cyst, would make it highly probable that it was an enterogenous cyst, which had undergone malignant degeneration.

In the fifth case there were no symptoms whatever attributable to the mesenteric cysts. During an examination of a patient suffering from an attack of acute appendicitis, a movable, tense, cystic, non-tender abdominal

* Dr. James Ewing was kind enough to review the case histories and pathological reports in this series of cases. In Case II, he agreed that the mesenteric cyst was probably of nephrogenic origin.

tumor was felt. The patient had known of its presence for a number of years. A pre-operative diagnosis of mesenteric cyst was made and recorded, and on the following day was confirmed at operation. A tumor mass, consisting of three mesenteric cysts in the lower abdomen, was delivered and the cysts enucleated. The clinical diagnosis was *dermoid cysts* of the mesentery, but the pathologist, Doctor MacNeal, while not positive, says they are probably tuberculous.

Treatment.—The treatment of mesenteric cysts can be considered under the following headings: (1) Enucleation; (2) resection; and (3) drainage.

(1) *Enucleation.*—This is the ideal operation and should be the method of choice when and where it can be accomplished without damage to the bowel or to the vascular supply thereof. From a study of the reported cases it is probable that this procedure is applicable in about one-third of all cases. Flynn gives the mortality following this operation at about 16 per cent. Enucleation could be done in but one of my cases.

(2) *Resection.*—By resection is meant the extirpation of the cyst or cysts and the resection of the involved bowel, with the establishment of some type of intestinal anastomosis. This operation is called for often—probably in one-fourth to one-third of the cases encountered. Unfortunately the mortality following resection is high—about 60 per cent. This can be explained by the fact that many of the emergency operations in which it is done are performed for the relief of acute intestinal obstruction, or in the presence of acute peritonitis. It is indicated when a successful enucleation cannot be completed and when marsupialization–drainage does not relieve or is apt to be followed by intestinal obstruction. Resection was performed in two, or 40 per cent, of my cases.

(3) *Drainage.*—When the size of the cyst or dense intestinal adhesions or other complications make the removal of the tumor a dangerous procedure, then some form of drainage of the cyst is called for. Simple wick or tube drainage is, in my opinion, inferior to gauze packing of the cyst cavity. Carter, Swartley, and others consider marsupialization obsolete, save in very exceptional instances. Flynn thinks it applicable only in parasitic cysts or in large unilocular cysts where the removal of the tumor is extremely hazardous. Despite the immediate theoretical dangers (of infection, peritonitis, intestinal obstruction) and the possible remote complications (recurrence of the cyst, persistent sinus, hernia, late intestinal obstruction, *etc.*) a study of the many isolated cases—reports in which this method was used, with both early and late good results—is convincing proof that the objections to it are more fanciful than real. It should never be employed in dermoid cysts nor as a make-shift or "way out" when enucleation can be accomplished or when resection is indicated. It is relatively safe and simple, with a mortality of only about 6 per cent., and a morbidity that is surprisingly slight. The gratifying outcome in my second case, in which no other plan of treatment seemed feasible, is offered as evidence of its value.

Is there no other plan of surgical treatment to be employed, when enucleation cannot be done; when resection, with its high mortality, should be avoided; and when drainage with its protracted convalescence, is deemed inadvisable? It is fully established that such cysts as sebaceous, dermoid, including the piloninal variety, hydatidiform cysts, mid-line and lateral embryonic cysts of the neck, *etc.*, require complete extirpation, otherwise there will be recurrence of the cyst or a persistent sinus will follow. Such half-way measures as incision, cauterization, packing or incomplete removal of the cyst will practically always result in failure to effect a cure. On the other hand there are many types of simple cyst that will heal after ordinary drainage operations. A most striking example can be cited in simple, uncomplicated hydrocele of the tunica vaginalis. Aspiration–injection, marsupialization–drainage, and resection or eversion of the hydrocele sac are methods that have been and still are being used in the successful treatment of this condition. It is my belief (based on my experience in my first and second cases of mesenteric cyst), in selected instances of single, thin-walled, serous, sanguineous or chylous cysts, the removal of the greater part of the cyst membrane, with closure of the incision in the mesentery, bringing the remaining segment of cyst in contact with the raw surface of the mesentery—that it will prove to be a perfectly satisfactory operation. It could be modified by placing a simple wick or cigarette drain into the intramesenteric space, from which the cyst was removed, but the first suggestion, of closure without drainage, is believed to be a better one.

CONCLUSIONS.—In June, 1927, the excellent article of Swartley, of Philadelphia, was published, giving a comprehensive review of the whole subject and bringing up-to-date the most recent opinions on the genesis, classification, diagnosis, and management of mesenteric cysts. Before his paper appeared I had stumbled upon three such cases and had operated upon them without ever having considered the possibility of such a surgical condition. The text-books consulted at that time gave little or no information on the subject, and the same is largely true today.

The impressions gained from my own experience and from a rather extensive study of the literature on mesenteric cysts are:

(1) If all the cases met with in practice could be put on record, the condition would no longer be considered rare—only relatively rare.

(2) Unless teachers of surgery make occasional mention of and unless future works on surgery place more emphasis upon this topic, failures to make correct pre-operative diagnoses will continue to be the rule and surgical mortality and morbidity will remain unnecessarily high.

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SODIUM RICINOLEATE

ITS POSSIBLE VALUE IN THE PREVENTION AND TREATMENT OF PERITONITIS

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THE value of soaps as germicidal agents has been frequently stressed. According to Walker,[1] "Koch first found that soap solutions possessed germicidal properties. Koch did not use chemically pure soaps, commercial soaps only being utilized. The first systematic work with chemically pure soaps was done by Reichenbach, who found potassium stearate, palmitate and myristate were germicidal to *Bacillus coli*." Walker found that pneumococci and streptococci were easily killed by sodium laurate and that while *Bacillus typhosis* was somewhat resistant, *Streptococcus aureus* was little affected by this soap. Nichols[2] showed that 0.5 per cent. sodium oleate, sodium resonate or "brown soap," in dish water, killed *Streptococcus pyogenes, Bacillus influenzæ* and pneumococcus. Reasoner[3] showed that shaving soap lather killed T. pallidum immediately. Walker[4] found cocoanut oil soap to be germicidal to *Bacillus typhosis* when used in washing hands. Tilley and Schaffer[5] found the germicidal ability of cocoanut oil to be increased by the addition of sodium chloride. Page and Allen[6] found that repeated intraperitoneal injections of soap solutions produced pathological changes, usually mild, and probably in a large degree non-specific. Recently, a highly purified soap, sodium ricinoleate, has been found to be bactericidal, inhibitory to bacterial growth and to be effective in detoxifying many toxins and endotoxins. These toxins while rendered non-toxic, are not destroyed, and in combination with the soap they retain antigenic properties that make them valuable in producing active immunization. It is the purpose of this paper to review the work with sodium ricinoleate and to point out some of its properties that may make it of value in its use in the prevention and treatment of peritonitis.

Larson and Montank,[7] in 1923, studying the effect of wetting on the viability and pathogenicity of the tubercule bacillus, noted that cultures grown in media containing sufficient sodium ricinoleate to depress the surface tension to 44 dynes were not so virulent to guinea-pigs as cultures grown under ordinary conditions. This prompted them to investigate the effect of 2 per cent. sodium ricinoleate on the pathogenicity of tubercule bacilli in sputum. Equal parts of 2 per cent. sodium ricinoleate and sputum containing tubercule bacilli which had stood for several hours after mixing, when injected into animals caused only a local lymphadenitis that subsided in fourteen days without any signs of tuberculosis. Controls injected with half the volume of untreated sputum all died.

Larson and Nelson[8] then discovered that sodium ricinoleate completely detoxified tetanus toxin and diphtheria toxin. Guinea-pigs were not affected by one hundred lethal doses of the respective toxins when the soap was added. This caused Larson, Evans and Nelson[9] to study the value of soap-toxin mixtures as antigens. Rabbits and guinea-pigs treated with soap-toxin mixtures were rendered immune and th the serum of rabbits

was found to have a high titre of antibodies against tetanus toxin. Guinea-pigs were immunized against both tetanus toxin and diphtheria toxin. They made the important observation that toxins were not only detoxified, but that their antigenic properties were not affected by sodium ricinoleate. Larson and Nelson[10] later found that if a solution of sodium ricinoleate was added to a virulent culture of pneumococcus, so that the final dilution of soap was 0.1 per cent., the microörganisms lost their pathogenicity instantly. Twenty-four hours after the intraperitoneal injection of such a mixture into rabbits, large amounts of agglutinins were present in the blood-stream, and the animals were resistant to many times the lethal dose of pneumococci. The serum of rabbits thus immunized protected normal rabbits against intraperitoneal and intravenous infections. A strain of *Streptococcus scarletinæ* lost its power to grow upon culture media when treated with 0.5 per cent. sodium ricinoleate for less than five minutes. Streptococci thus treated produced agglutinins in rabbits within twenty-four hours after intraperitoneal injection.

Larson and Colby[11] then prepared scarlet toxin, the potency of which was 15,000 skin doses per cubic centimetre, and added sodium ricinoleate so that the final dilution of the soap was 1 per cent. Very encouraging results in immunization of children against scarlet fever were obtained with the intramuscular injection of varying amounts of this solution. Ninety-six per cent. of 132 children gave a negative Dick reaction three weeks after they had received a single dose. A mild local reaction followed the injection in 15 per cent. of these cases. Larson, Hancock and Eder[12] reported successful immunization of children against diphtheria by mixtures of sodium ricinoleate and diphtheria toxin. Larson and Eder[13] later reported on immunization against diphtheria and concluded that the mixture of soap and toxin was superior to that of toxin-antitoxin and also that it had the additional advantage of eliminating horse serum. Larson, Huenekens and Colby[14] then reported the further use of sodium ricinoleate and scarlet-fever toxin in immunization. The fact that 77.3 per cent. of those treated were negative to skin test after eight days suggested the use of the mixture in suppressing an epidemic of scarlet fever.

In the earlier paper of Larson and Colby[11] 48 per cent. of cases receiving a single dose gave a negative skin test after five days. Since this time large numbers of children have been thus successfully immunized against scarlet fever and diphtheria by the use of three injections at seven-day intervals. During 1927 Larson and his assistants successfully immunized children against scarlet fever and diphtheria by using a mixture of the toxins of both scarlet fever and diphtheria and sodium ricinoleate. Three doses at weekly intervals were given. Since that time Larson has immunized several thousand children against these diseases. Other workers have reported similar success.

Carmichael,[15] interested in the toxic properties of ricin, a powerful vegetable toxin, found that 200 lethal doses of ricin, to which was added 0.4 grams of sodium ricinoleate, was rendered non-toxic to laboratory animals. Immunity to ricin developed after a single injection of the soap-toxin mixture. He also noted that the sera of animals treated with soap-toxin mixtures had antiricin properties. Carmichael[16] further found that five lethal doses of rattlesnake venom was rendered non-toxic to rabbits when treated with sodium ricinoleate *in vitro*. He also detoxified rattlesnake venom by leaving the needle at the site of injection and introducing sodium ricinoleate thirty minutes later.

McKinley and Larson[17] obtained a sample of the "M. A." strain of poliomyelitis and produced poliomyelitis in monkeys. Monkeys thus affected were killed at the height of the disease and an emulsion of brain tissue was prepared in 1 per cent. sodium ricinoleate. This solution produced active immunity in normal animals. Although their series was small the authors concluded that it demonstrated a possible method of immunization against poliomyelitis.

Netter, Andre, Cesari and Cotoni,[18] in France, confirmed Larson's findings of the effect of sodium ricinoleate on the organisms of anthrax, tuberculosis, and on the toxins of *Bacillus tetani*, *Bacillus diphtheriæ* and *Streptococcus scarletinæ*. Netter, Coshni and Cotoni[19] confirmed Larson's findings on the effect of sodium ricinoleate on the toxins

of streptococci and pneumococci. Cotoni and Cesari[20] and Renaud,[21] reported further on sodium ricinoleate.

Halvorsan,[22] in 1925, reported the method used by Larson in preparation of his soap. Kozlowski[23] attempted to substantiate Larson's findings, using a solution of sodium ricinoleate that he had prepared, and concluded that the soap was too toxic for clinical use. He produced ulceration at the site of injection and killed a large number of mice with solutions that contained 2 per cent. of sodium ricinoleate. This article was responded to by Larson[24] who pointed out that Kozlowski had prepared his soap by purifying the ricinoleic acid through the barium salts.

The barium was apparently the cause of the ulceration and toxic effect. Larson[25] had discontinued this method of preparation of his soap and for several years has used isopropyl alcohol to remove all the non-saturated fatty acids. That the reaction of subcutaneous tissues to the solutions of sodium ricinoleate used by Larson must be slight was shown by Ekola.[26] Soap and diphtheria toxin-soap vaccines were found to be but slightly more irritating to subcutaneous tissues than trypan blue, which is considered the least toxic of the vital dyes. Diphtheria toxin alone produced more necrosis than the soap or soap-toxin mixture used. This was a histological study of injected rabbits. Larson[27] stated that he had rarely seen abscess formation after injection of sodium ricinoleate. He quoted Green who stated he had practically never seen an abscess after more than one hundred thousand injections into foxes, of a distemper vaccine containing sodium ricinoleate. Green, Ziegler, Green and Dewey,[28] in 1928, used ricinoleated virus for active immunization of several thousand foxes, with resultant lowering of the mortality rate.

Kozlowski[29] later reported the action of sodium ricinoleate upon several bacteria. He found that streptococci isolated from cases of erysipelas, measles and scarlet fever were killed by this soap in a dilution of 1 : 5000 in seven hours, or sooner at 35° C. while in control cultures, without soap, they survived for more than a week.

Their growth was inhibited by this soap in a dilution of 1 : 20,000. Pneumococci were readily dissolved by sodium ricinoleate in a dilution of 1 : 5000. He found that *Bacillus paratyphosis, Bacillus dysenteriæ, Bacillus coli-communis* and *Streptococcus fæcalis* were quite resistant to the inhibitory and bactericidal action of sodium ricinoleate. Larson[8] had noted that botulinis toxin was more resistant to sodium ricinoleate than tetanus toxin or diphtheria toxin. He assumed that this offered a possible explanation to the fact that neither diphtheria toxin nor tetanus toxin is absorbed in toxic form from the intestinal tract, while botulinis toxin is readily absorbed by the digestive organs. The contents of the intestinal tract have a low surface tension because of bile and soaps present which probably destroy tetanus and diphtheria toxins but not botulinis toxin. This also recalls the lytic action of bile on the pneumococcus. Kozlowski[29] suggested that sodium ricinoleate might be used instead of bile in dissolving pneumococci in diagnostic routine work. However Spencer[30] in an extensive study of the visible effect of sodium ricinoleate on suspensions of eighty-three species of bacteria tested his cultures of pneumococci several times and found that they were only slightly cleared. He found that *Bacterium tularense* suspensions completely cleared with a soap dilution of 1 : 800.

So far as his tests had been carried out the reaction of *Bacterium tularense* was unique and he suggested this effect as an additional criterion for identity of this organism.

This covers the work done with sodium ricinoleate prior to 1929, except that of Spencer and Ekola, which was done in 1929 and 1930.

While a student at the University of Minnesota in 1927, where Larson was working, I studied the rate of absorption of various substances from the peritoneal cavity of dogs. It occurred to me that the addition of sodium ricinoleate might aid the animals to survive the large amount of toxic exudate found in the peritoneal cavity after ligation, trauma or infection of the intes-

tines. Many substances, including sodium chloride solution, glucose, ether, pastes, and Dakin's solution, have been used in the peritoneal cavity to combat peritonitis. Most of these substances have been used for their bactericidal effect, some for their inhibitory effect on bacterial growth, others because they attract polymorphonuclear leucocytosis and still others were used simply empirically. No substance has been available that combined bactericidal, inhibitory and *detoxifying* powers until the introduction of sodium ricinoleate. I first suggested its use in peritonitis in 1928[31] and Larson very kindly furnished me with samples prepared in his laboratory.

The first animal experiments were done early in 1929. Frequent changes of station have interrupted my animal experimentation and I have not had access to a large number of clinical cases of peritonitis, so that I am deferring until later the detailed report of my own experience, offering at this time the general results and a review of the literature covering its clinical use with the hope of stimulating further study of the efficacy of sodium ricinoleate in the prevention and treatment of acute peritonitis.

Sodium ricinoleate has been used clinically by many workers. Early in 1925 Hartzell[32] recommended use of a paste containing sodium ricinoleate in the local treatment of tooth sockets. Since that time much has been written in dental journals on this subject.

Dorst and Morris[36] studied a large series of patients suffering for years with "irritable colon" some of whom had frequently been diagnosed chronic appendicitis, peptic ulcer, chronic cholecystitis, spastic colitis and mucous colitis. After many years of effort to isolate some unusual organism that might account for the condition, they investigated the normal flora of the intestinal tract. Twenty-six of thirty patients tested showed marked sensitivity of the skin to one or several of the "normal strains." The authors then attempted to desensitize these patients by giving small doses of autogenous vaccine.

The results were gratifying but the treatment required several months. Similar cases had responded well to repeated doses of castor oil, an effect attributed to the change of castor oil to ricinoleates in the intestinal tract. They therefore gave five-grain doses of sodium ricinoleate suspended in olive oil in capsules with better results than were obtained with the castor oil. They then prepared a ricinoleated vaccine from the "normal strains" of the intestinal flora and found that it was tolerated without local or focal reaction in doses five times those of the untreated vaccine. The combined treatment of sodium ricinoleate capsules by mouth and injections of ricinoleated vaccine gave very good results.

Kline[34] reported fifteen cases of tuberculous enteritis which were greatly benefited by oral administration of sodium ricinoleate in capsules.

Lutterloh and Stroud[35] were the first to introduce sodium ricinoleate solution into the peritoneal cavity clinically. They used 2 per cent. sodium ricinoleate in 1 per cent. sodium chloride, pouring it into the belly cavity at operation where ruptured appendices were encountered. They did not report the amount they used. They stated that convalescence was much less stormy and that patients were free from discomfort after operation, and that the mortality rate was very low.

They report the use of sodium ricinoleate solution in osteomyelitis and the local application in the form of saturated dressings in cases as treatment for extensive burns.

My experiments to date seem to warrant the following comments. There is a great variation in the solutions of sodium ricinoleate now available.

Samples obtained in 1928 from Larson were found to be non-toxic when 10 cubic centimetres of 2 per cent. solution was injected into the peritoneal cavity of guinea-pigs. Solutions were made up fresh each time that experiments were carried out. However, after the sample of sodium ricinoleate was several months old, 10 cubic centimetres of 2 per cent. solutions regularly killed guinea-pigs in a few hours, even though the precautions were followed to make the solutions with distilled water, and to keep them in hard glass containers to avoid chemical change. Solutions which were cloudy after mixing were found to be toxic. This probably resulted from changes in the samples. Samples must be prepared by a method which assures freedom from non-saturated acids or barium in the final product. Even though small amounts of sodium ricinoleate solution are tolerated well in the peritoneal cavity, the total amount injected is limited both by irritant and toxic effects. Two rabbits were injected with 15 cubic centimetres of 2 per cent. solution. One died in thirty-six hours and the other died in seventy-two hours. In the latter were found dense intestinal adhesions and a small amount of exudate, and in both cases the peritoneal cavity showed evidence of pronounced irritation. This irritation should not prevent utilization of sodium ricinoleate in weaker concentration since a mild irritation is considered beneficial in peritonitis, as a stimulant to attract polymorphonuclear leucocytes to the site of infection. Two rabbits were then injected with the same total dose, .3 gram of sodium ricinoleate, but in a dilute solution of 0.5 per cent. Both of these rabbits died within three hours. Two rabbits were injected with the same amount of 0.5 per cent. solution made up in normal saline, and died within two hours. This seems to warrant the assumption that the sodium ricinoleate was absorbed more rapidly in the dilute aqueous solution, since more peritoneal area was affected by the solution of greater quantity. Normal saline being a medium more nearly simulating body fluids probably facilitated the more rapid absorption of the toxic substance. However, small amounts of sodium ricinoleate have been injected into the peritoneal cavity hundreds of times by Larson and others and I have found small amounts to have no toxic effect. More detailed animal experiments will be reported later on the lethal dose. Many animals have been protected by the addition of sodium ricinoleate to cultures injected intraperitoneally. A broth culture of a streptococcus obtained from a fatal case of septicæmia was injected intraperitoneally into guinea-pigs, and death followed within forty-eight hours.

Equal amounts of the culture to which 1 cubic centimetre of 2 per cent. sodium ricinoleate was added in the syringe at the time of injection, proved less rapidly fatal, the animals living for several days. Preliminary work done on intraperitoneal injection of killed cultures of organisms, to which sodium ricinoleate was added, indicate that active immunization against the usual organisms soiling the peritoneal cavity might prove valuable in increasing the immunity to these organisms. This idea is based on the work of Herrman[36] and of Rankin and Bargen[37, 38] who have reduced operative mor-

tality by peritoneal vaccination prior to surgical procedures on the large bowel. It is believed that greater doses of vaccine may be given intraperitoneally if sodium ricinoleate has been added. The work of Dorst and Morris[33] indicates that oral administration of sodium ricinoleate prior to operation and in the presence of acute peritonitis may prove valuable in lowering operative mortality. As stated by Larson and others, streptococci and pneumococci are killed by sodium ricinoleate and large amounts of their toxins are rendered non-toxic. I have found sodium ricinoleate effective in killing a suspension of gonococci in 1:1,000,000 solution after three minutes contact in vitro. Clinically 0.5 per cent. sodium ricinoleate solution has given encouraging results in the treatment of gonorrheal urethritis, but the series is too small to warrant its recommendation without proven value in a large series of cases.

The unusual susceptibility of streptococci and pneumococci and their toxins to sodium ricinoleate suggests that sodium ricinoleate may be of value in the treatment of empyæma.

The work of Morris and Dorst[33] has shown that sodium ricinoleate is effective on the bacteria of the normal flora of the intestinal tract. The work of Larson and many others has shown that sodium ricinoleate is bactericidal to streptococci, pneumococci, *Bacillus diphtheriæ*, and that the toxins of these organisms are rendered non-toxic when sodium ricinoleate has been added in proper amounts. This indicates that we have a valuable substance in combating the organisms and toxins which account for the majority of fatal infections of the peritoneal cavity. Sodium ricinoleate would seem especially valuable in pneumococcic and gonococcic peritonitis. The use of an aqueous solution of sodium ricinoleate may not be the best. Lutterloh and Stroud[35] used 1 per cent. saline as a medium. My experience with normal saline as a medium tends to show that there is more danger than with aqueous solutions. Some work has been done on buffers, which is not ready for publication. The discovery of Johnson[39] that amniotic fluid spilled into the peritoneal cavity at the time of Cæserian section has resulted in a less stormy convalescence suggests that this may be a valuable diluent for sodium ricinoleate.

The action of sodium ricinoleate on toxins is believed by Larson to be an adsorptive phenomenon. Physical factors are involved which have not been explained. It would seem advisable therefore to seek a medium which is the most nearly a normal body fluid. Much experimental work must be done before sodium ricinoleate can be proven acceptable in the treatment of peritonitis. Clinical use will not be warranted until large series of animal experiments indicate the dosage, strength of solutions, diluents, time of administration, and limitations of this form of treatment. A series of animal experiments are now in progress which will be reported at a later date. Chemically pure sodium ricinoleate has been recently put on the market commercially.[40]

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INTERNAL HERNIA FOLLOWING POSTERIOR GASTROENTEROSTOMY*

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A HERNIA is variously defined as: (1) A rupture; (2) the protrusion of an organ or part of an organ or other structure through the wall of the cavity normally containing it; (3) the protrusion of a loop or knuckle of an organ or tissue through an abnormal opening; (4) the protrusion of peritoneum liable to contain, containing at times, or permanently containing any viscus or part of a viscus from the abdominal cavity.

No one of these definitions satisfies all types of hernia, as is quite evident when we consider that condition in which loops of small intestine pass through the Foramen of Winslow into the lesser peritoneal cavity. Yet I think we will all agree in calling such a condition a hernia. It is the general conception that a hernia must possess a sac lined by peritoneum and if this is the true definition, the condition which I am about to describe cannot be classed as a hernia, but as an incarceration or strangulation, depending on the circulation of the bowel.

I shall proceed first to the description of my case and then briefly review the other cases found in the literature.

L. S., male, aged thirty-two years. Steelworker, was admitted to the Mercy Hospital on the night of March 3, 1929. He gave a history of indigestion dating back four years. Twenty-four hours previous to admission he had epigastric pains lasting four hours. Twelve hours before admission the pains returned with increased violence and he began to vomit. He was seen by a physician who administered morphine and prescribed ice to the abdomen without relief. Physical examination on admission revealed a flat abdomen, generalized rigidity—boardlike in the epigrastrium—and marked tenderness. Pulse, 96; temperature, 98.6°; blood-pressure, 138/90.

Under diagnosis of perforated gastric ulcer the abdomen was opened. On the anterior wall of the duodenum just outside the pylorus was an ulcer the size of a five-cent piece with a perforation the size of a slate pencil. Ten ounces of bile and gastric secretion were obtained by passing an aspirator to all parts of the abdomen. The ulcer was excised by cautery and closed with silk. The duodenum was so narrowed that a posterior short loop retrocolic gastroenterostomy was performed. The opening in the transverse mesocolon was anchored about the anastomosis and the abdomen closed without drainage. Six hours after the operation he vomited thirty-five ounces of bile-stained fluid and smaller amounts during the first three days. Nine days after operation, during an attack of coughing, the wound opened, forcing out a piece of omentum. Secondary suture of the wound was required. His general condition, however, remained good till early in the morning of the eighteenth day. There had been no recurrence of the vomiting since the third day; bowels were moving twice a day naturally and he was taking a liberal diet. Suddenly he was seized with violent

*Read before the Pittsburgh Academy of Medicine, March 22, 1932.

abdominal pain, chiefly in the left hypochondrium. The pains were intermittent and he vomited large quantities of bile-stained fluid. The upper abdomen was somewhat rigid, chiefly on the left side. Tenderness and fullness in this region were accentuated during the pains. A diagnosis of acute intestinal obstruction was made and under ether anæsthesia, the abdomen was again opened about ten hours after the onset of pain through a left upper rectus incision.

A loop of slightly distended, congested jejunum, about three feet in length, was found in the left hypochondrium. It had passed from right to left between the afferent loop of jejunum and the lower leaf of the transverse mesocolon, thus forming an

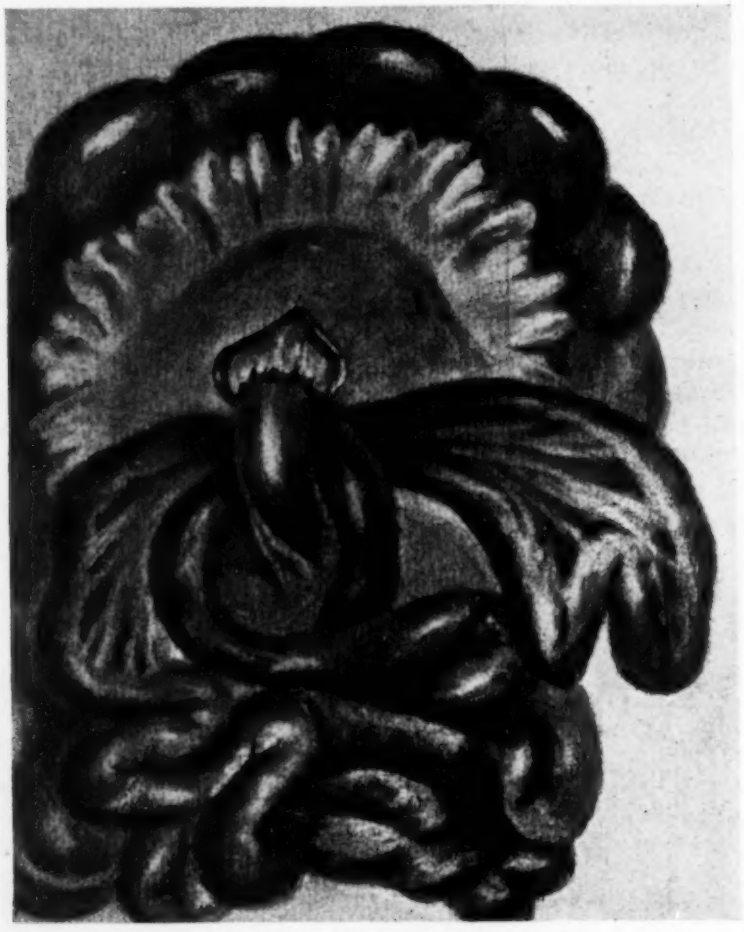

FIG. 1.—Internal hernia of jejunum.

internal hernia (Fig. 1). This was easily reduced. The weight of this loop of bowel had produced a kink in the jejunum just opposite the anastomosis with a resulting vicious circle. To prevent a recurrence of the hernia, the proximal loop of jejunum was anchored to the lower leaf of the transverse mesocolon with one suture. An entero-anastomosis between the proximal and distal loops was performed to prevent any recurrence of the vicious circle. Convalescence was uneventful. He was discharged from the hospital six weeks after admission. He returned to work nine days after leaving the hospital and during the first five and one-half months lost only one day.

On November 3, 1929 (eight months after his first admission), he was re-admitted

to the Mercy Hospital with a history of pains dating back two months. During the last month they had been especially severe, occurring daily just after meals, frequently accompanied by vomiting and not relieved by diet or medication. A diagnosis of marginal ulcer was made although confirmation could not be obtained by X-ray.

November 13, ten days after admission, the abdomen was opened for the third time. There was an ulcer of the jejunum less than an inch distal to the gastro-jejunostomy. It had perforated the bowel, forming a crater the size of a dime on the under-surface of the transverse colon. The original duodenal ulcer showed only a very faint scar. The gastroenterostomy was torn down and the openings in the stomach and bowel closed, thus reëstablishing the normal tract. The wound healed by primary union. Convalescence was uneventful and the patient was discharged from the hospital sixteen days after operation. Twelve days later he requested that he be permitted to do light work. A few weeks ago I saw this patient and he again has mild symptoms of duodenal ulcer.

For many years the possibility of a herniation through the opening of the transverse mesocolon into the lesser peritoneal cavity has been recognized. To prevent such a complication following posterior gastroenterostomy it has become a universal custom to anchor the margins of the opening in the transverse mesocolon about the anastomosis.

Herniation of small intestine between the proximal loop of jejunum and transverse mesocolon has occurred so rarely that preventive steps are seldom taken unless the surgeon has had such a case. All that is necessary is the obliteration of the opening by one or two sutures anchoring the proximal jejunal loop to the under-surface of the transverse mesocolon.

In 1915, Moschcowitz and Wilensky collected two cases complicating anterior long-loop gastroenterostomy (Peterson, Mayo) and six cases complicating short-loop retrocolic anastomosis (Steudel, Peterson, Gray, Gordon, Barker, Moschcowitz and Wilensky). To these, Fowler has added three cases complicating short-loop (Ashhurst, Bryan, Fowler). The author has discovered two other case reports, one by Winkelbauer complicating short-loop retrocolic anastomosis and the other by Steden complicating long-loop antecolic gastroenterostomy.

The complete list comprising eleven cases complicating short-loop and three cases complicating long-loop operations is given in the opposite table, together with the essential facts where available.

Although many theories have been advanced as to the etiology of this unusual complication, most of them are fantastic and far-fetched. From the study of the cases reported a number of interesting points are discovered. W. J. Mayo stated thirty years ago that the danger is much greater with the anterior long-loop operation than with the posterior short-loop anastomosis. That statistics do not bear out this statement is probably due to the fact that anterior gastroenterostomy is now but rarely performed. Of the twelve cases where the direction of the passage of the loop is mentioned, in all but one was it from right to left. Where the retrocolic anastomosis was employed, the complication occurred in all but one case within the first three weeks, whereas in two of the three long-loop antecolic anastomoses, the incarceration did not occur till one year and nine months respectively after the original operation. Almost always within the first few days after the retrocolic anastomosis there is vomiting of massive

TABLE.—HERNIATION OF SMALL INTESTINE

Reference	Internal Primary Condition	Primary Operation	Diagnosis of Hernia Made by	Elapsed Time After Anastomosis	Direction of Passage of Loop	Length of Incarcerated Loop	Result
Steudel	Cancer	Resection and posterior gastroenterostomy with Murphy button	Autopsy	17 days	Right to left	Short loop	Death
Peterson	Cancer	Resection and anterior anastomosis with Murphy button	Autopsy	6 days	Right to left	Most of small bowel	Death
Peterson	Cancer	Posterior gastroenterostomy	Autopsy	10 days	Right to left	All small intestine	Death
W. J. Mayo	Ulcer lesser curvature	Anterior gastroenterostomy with Murphy button	Operation	1 year later	Right to left	More than half small intestine	——
Gray	Ulcer	Posterior short loop gastroenterostomy	Operation	6 days	Left to right	All small intestine	Recovery
Gordon	——	Posterior gastroenterostomy	Operation	———	Right to left	————	Recovery
Barker	——	Posterior gastroenterostomy	Operation	2 years	————	All small intestine	Recovery
Moschcowitz and Wilensky	Ulcer	Posterior gastroenterostomy	Operation	14 days	Right to left	Most of small intestine	Death
Bryan	Perforated duodenal ulcer	Posterior gastroenterostomy	Operation	12 days	Right to left	All small intestine	Recovery
			Second operation for recurrence	6 days	Right to left	? Small intestine	
Fowler	Ulcer lesser curvature	Posterior gastroenterostomy	Operation	12 days	Right to left	1 foot	Recovery
Steden	Perforated gastric ulcer	Anterior gastroenterostomy	Operation	9 months	Right to left	Most all small intestine	Death
Winkelbauer	Duodenal ulcer	Resection and retrocolic end to side	Operation	9 days	Right to left	Most all small intestine	Death
Buchanan	Perforated duodenal ulcer	Posterior gastroenterostomy	Operation	18 days	Right to left	About three feet	Recovery
H. C. Deaver**	Carcinoma	Anterior long loop gastroenterostomy	Autopsy	———	————	————	Death

** By personal communication with Dr. Astley P. C. Ashhurst.

quantities of bile-stained fluid, indicating a vicious circle with dilatation from improper drainage. In eight of the cases almost the entire small bowel was incarcerated. In the other four cases, where any mention is made, the length of the loop varied from one foot to half the small intestine. Frequently the condition is ushered in with collapse not associated with pain. The degree of shock probably depends on the length of the incarcerated loop together with the amount of interference to its blood supply. A number of the patients, however, experienced pain and all the symptoms of acute obstruction.

While vomiting and coughing probably play some part in the production of internal hernia, they occur so commonly and the complication under discussion so rarely, that there are undoubtedly other factors of which we have no absolute knowledge.

Bryan's case is the only one where there was a recurrence of the condition. The first hernia appeared twelve days after the gastroenterostomy and the second six days later. At the second operation to prevent recurrence he not only closed the opening as is generally advised, but performed enteroanastomosis and sutured the descending loop to the parietal peritoneum.

In conclusion, I may state that internal hernia or incarceration of small intestine complicating short-loop retrocolic anastomosis is a rare condition. The factors producing it have never been satisfactorily explained. It is generally preceded by the vomiting of large quantities of bile. It usually occurs from one to three weeks following operation. There may be collapse without pain or pain and all the symptoms of intestinal obstruction. The only treatment is early operation. The preventive treatment is the obliteration of the fissure by one or two sutures between the proximal loop and the lower leaf of the transverse mesocolon.

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POSTERIOR PITUITARY EXTRACT IN THE PREVENTION OF POST-OPERATIVE INTESTINAL DISTENSION

A PRELIMINARY REPORT*

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Post-operative paralytic ileus is one of the major complications of abdominal surgery. Preceding any true ileus there are varying grades of intestinal distension. This distension is primarily due to a loss of tone of the smooth muscle of the intestinal tract caused by changes in intra-abdominal pressure, handling of the viscera, changes in temperature, the anæsthetic, morphine, and the presence of infection within the peritoneal cavity. This atonia varies in degree and duration and is most often encountered in the presence of peritonitis. Much has been written concerning the treatment of post-operative distension and ileus once these complications have arisen, but there is little to be found in the literature concerning means for their prevention.

Some three years ago a study was undertaken on the wards of the First Surgical Division, Bellevue Hospital, the object of which was to work out, if possible, a method for the prevention of post-operative distension, hence paralytic ileus. It was felt that if the tone of the intestine could be maintained during the first few post-operative days—in other words, through the atonic period—the smooth muscle could then resume its normal function.

To arrive at some idea of the prevalence of post-operative distension, 100 consecutive cases of acute appendicitis were reviewed. In 40 per cent. of these cases there was sufficient distension during the first three post-operative days to require the use of enemas, irrigations, rectal tubes or stupes. There were two cases of paralytic ileus. Twenty-one of these patients had to be catheterized.

The employment of posterior pituitary extract has been recommended for many years in the treatment of distension and ileus. Its action on distended intestine is sometimes violent and of short duration and some surgeons have advised against its use, fearing that any undue activity of the intestine might spread an existing peritonitis or blow out an appendix stump.

In 1924, in a paper on "Suppurative Peritonitis," Dr. Joseph A. Blake recommended the use of pituitary extract as a preventive routine, one ampoule of surgical pituitrin to be given after operation and continued at intervals of four hours for six doses, or more if indicated.

* Read before the New York Surgical Society, December 9, 1931.

In 100 abdominal cases of various types, this routine was followed. It was found that, whereas the incidence of post-operative distension was materially lessened, there were certain cases in which distension continued to be a problem. These could be classified under two headings: first, those in which considerable gas was present in the intestine at the end of the operation and before the administration of the initial dose of pituitrin; and second, those in which distension appeared after the final dose of pituitrin had been given. It was evident that in certain cases pituitrin had been started too late and that in others its use had not been sufficiently prolonged. The latter conclusion applied particularly to the cases of suppurative peritonitis. In the cases in which pituitrin had been given in the absence of distension, notably following spinal anæsthesia, clinically there was no indication of increased peristalsis, the effect of the drug being merely to maintain normal tone. The patients complained of no discomfort such as might be attributed to any violent activity of the intestinal musculature.

In 1928, Dr. Oliver Kamm and his co-workers isolated the alpha and beta hormones of posterior pituitary. The beta hormone has the vasopressor activity of the old pituitrin. It lacks the oxytocic or uterine. As this preparation, introduced under the name "Pitressin," seemed more specific for our purposes, it was substituted for pituitrin in our next series.

In our previous work, we had found that the two types of case in which post-operative distension was most apt to appear as a complication were acute appendicitis with or without peritonitis, and diseases of the biliary tract. It was therefore determined to limit our further observations to these two groups. It was felt that in cases operated upon under spinal anæsthesia, with its accompanying intestinal constriction, the first dose of pituitary extract could safely be given directly following operation, whereas with general anæsthesia the initial dose must be administered before operation. In the latter case, aside from forestalling any distension which might occur during operation, we hoped to be enabled to observe at first hand the action of the drug on the intestinal tract and to determine whether there was increased peristalsis or merely a maintenance of or slight increase in the existing tone of the intestine, as had appeared to be the case clinically. From our earlier observations we felt that the major effect would be found to be on the musculature of the small intestine rather than on that of the stomach or large intestine.

The second series was composed of fifty cases operated upon for acute appendicitis and fifty cases operated upon for biliary disease. In six of the former there was an accompanying spreading peritonitis and in eleven there was a localized peritoneal abscess. The routine as regarded pituitary extract was as follows: in the cases operated upon under spinal anæsthesia, an initial dose of pitressin was given intramuscularly directly following operation, and continued every four hours for eight doses in the case of uncomplicated appendicitis, for twelve doses in the biliary cases, and for fifteen doses or more where acute appendicitis was complicated by peritonitis. In two cases

of spreading peritonitis, pitressin was administered every four hours for twenty-eight and thirty-six doses respectively. All cases were carefully observed and evidences of intestinal distension, inability to void, and post-operative shock were noted. In twelve cases operated upon under general anæsthesia (avertin plus gas-oxygen) observations on the action of the drug in the open abdomen were made.

The results in this series were as follows: In ninety out of the hundred cases there was no evident distension. Of the remaining ten cases, eight became moderately distended following the final dose of pitressin. In one of the biliary cases there was marked distension. This patient was extremely stout and there appeared to be no effect from the administration of the drug. In the remaining case, one of acute appendicitis with peritoneal abscess, the distension was the result of a mechanical obstruction and an ileostomy was necessary. Seven patients were catheterized. In six of these spinal anæsthesia had been employed. There was no instance of post-operative shock. In no case, save that in which there existed a mechanical obstruction, was there any outward evidence of increased peristalsis. The action of the drug, as in our previous series, appeared to be that of merely maintaining tone.

In the appendicitis series there were two deaths. The first was a case of spreading peritonitis who died on the eighth day with extreme jaundice, the result of multiple liver abscesses, proved at autopsy. The second was referred to above—a late case with localized peritonitis and mechanical obstruction. This patient was sixty-five years of age and the immediate cause of death was bilateral bronchopneumonia. Autopsy revealed a band constricting the terminal ileum adjacent to the wall of the abscess. In the biliary series there were three deaths. The first was a case of common-duct stone in which death was due to pneumonia. In the second a choledochoduodenostomy had been performed for carcinoma of the head of the pancreas with stenosis of the cystic duct. Death was due to peritonitis. The third case was one of chronic cholecystitis with stones in the gall-bladder. Death was thought to be the result of a mesenteric thrombosis, although this could not be proved as further operation was refused and an autopsy was not obtained.

In twelve cases of biliary disease operated upon under general anæsthesia, an opportunity was had of observing the action of pituitary extract. In eleven of these cases a gradual generalized shrinkage of the small intestine was noted, but not of the degree seen following spinal anæsthesia. This came on between ten and twenty minutes following the intramuscular administration of pitressin, was not peristaltic in type, and remained throughout the operation. It made, in all instances, for an extremely easy closure. In one case there was no visible contracture of the small intestine. In none of these twelve cases was any effect on the musculature of the stomach or large intestine noted.

CONCLUSIONS

The prophylactic use of posterior pituitary extract has proved an effective means of minimizing post-operative abdominal distension.

When administered before the onset of intestinal smooth muscle relaxation, the result is a quiet abdomen, there being no evidence of increased peristalsis.

In 200 cases in which pituitary extract has been used as routine, no untoward results have been noted.

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X-RAY DIAGNOSIS OF ACUTE INTESTINAL OBSTRUCTION WITHOUT THE USE OF CONTRAST MEDIA

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The method of X-ray diagnosis of acute intestinal obstruction by studies of the gas distribution and fluid levels is by no means a new one. Its use, however, is apparently not as widespread as its importance would seem to warrant. Writers on the subject of intestinal obstruction have been almost unanimous in deploring the late diagnosis and tendency to procrastination which keeps the mortality in this condition at its present high figures. In our hands the plain röntgenogram has proven a valuable, if not infallible, aid to diagnosis, and has been the determining factor leading to immediate operative intervention in cases clinically doubtful. Thus we have at times been able to avoid that period of observation during which the chances of the patient's recovery diminishes with the increasing clarity of the diagnosis. On the other hand, in cases where the diagnosis of obstruction was seriously considered, but where the röntgenological signs necessary for the diagnosis of mechanical occlusion were absent, it has resulted in the avoidance of unnecessary exploration. Another important virtue of this method is, that by enabling us to differentiate between obstruction of the colon and of the small bowel it has made it possible for us to determine pre-operatively upon the type of procedure which would give relief with minimal shock and manipulation.

It should by this time be unnecessary to caution against the oral administration of barium in cases of suspected intestinal obstruction, but the author has seen three cases in the past year where an acute obstruction was precipitated following an opaque meal.

The most complete and accurate data for röntgenological study will be obtained if plates are taken in the following three positions:

(1) With the patient lying on his back and the plate behind him—this gives the best conception of the topographical relation of the coils of small bowel to each other and to the large bowel. (Fig. 3.) In stout people, however, and in patients in whom there is as yet little distension, the presence of abnormal gas accumulations may be missed.

(2) With the patient lying on his abdomen and the plate beneath him—this position gives the sharpest definition of intra-intestinal gas and bowel outline. Its disadvantage is that dilated loops of small bowel may be displaced into the flanks by the pressure against the central portion of the abdomen interfering in the differentiation between colon and small bowel. (Figs. 1–4.)

(3) With the patient in the erect posture—this will permit the demonstration of fluid levels in the bowel by causing the gaseous contents to rise on top of the liquid contents. (Figs. 2–6.) In patients too sick to sit up Ochsner's suggestion of taking

plates with the patient lying on his side with the plate against his abdomen has proven satisfactory.

The plates should be taken before the administration of enemata or irrigation of the colon for the following reasons: In the first place the gas which may be present in the colon may be expelled, and a wrong conception of the type of gas distribution obtained. In the second place if the plate is taken too soon after the irrigation, retained fluid and gas introduced by it may not be completely absorbed or expelled, and may give rise to small fluid levels in the colonic saccules.

The following communication is based on the study of fifty-nine cases of acute mechanical occlusion of the bowel diagnosed as such röntgenologically and proven to be such by operation. Of these, the obstruction was in the ileum in thirty-nine cases, and in the colon in twenty. In addition, there have been an almost equal number of cases where the subsequent clinical course, operation or autopsy confirmed the X-ray conclusion that mechanical ileus was absent. In some of these cases the distension was definitely known not to be due to mechanical ileus, but studies were made in order to determine what portions of the bowel were mainly concerned in giving rise to the abdominal distension.

Acute Mechanical Occlusion of the Small Intestine.—Under *normal* conditions in the *adult* gas cannot be röntgenologically demonstrated in the small bowel. In the colon, however, it is a matter of every-day observation to note varying quantities of gas usually sufficient in amount to outline its distinctive markings and course. In neither portion of the bowel can fluid levels be demonstrated. When acute mechanical occlusion from any cause occurs in the small bowel, the gut proximal to the site of obstruction very rapidly becomes distended with gas and fluid. Distally, the entire enteric tract including the colon becomes empty and collapsed. Röntgenologically, this pathological alteration is mirrored by the following findings:

(1) Presence of dilated coils of small bowel (normally absent).
(2) Absence of gas in the colon (normally present).
(3) Presence of fluid levels in the small bowel.

In our experience, the earliest sign to appear is the development of fluid levels. It was present in two cases where no dilatation of the small bowel could be demonstrated in the flat plate.

Aside from the two cases just mentioned, all of the thirty-seven proven cases of acute small bowel obstruction had these diagnostic signs. In no case where these signs were absent was the subsequent course one of acute mechanical obstruction. On the other hand, and this is important, from the standpoint of operative intervention, these signs are *not* absolutely pathognomonic of *mechanical* obstruction. We have observed these signs a number of times in cases of peritonitis and in severe post-operative paralytic ileus. (This point will be discussed again later.) At this juncture we must also note the exception provided by two cases of strangulated partial enterocele in which small globules of gas could be visualized in the colon together with distended coils of small bowel and fluid levels. (Fig. 9.)

FIG. 1.

FIG. 2.

FIG. 1.—Obstruction of the small bowel of two days' standing. Plate taken with patient lying on abdomen; the characteristic serrated ribbed appearance of the small bowel is well shown. Small bowel has been displaced into the flanks.

FIG. 2.—Fluid levels in an early obstruction of the small bowel.

FIG. 3.

FIG. 4.

FIG. 3.—Classical example of small bowel obstruction, parallel loops of small bowel arranged in a ladder pattern. Obstruction twenty-four hours' duration due to band from previous appendix operation. Plate taken with patient on back.

FIG. 4.—Obstruction of the small intestine near the ileo-cæcal angle. Same patient as above. Plate taken with patient on abdomen. Gut displaced into flanks.

In order to facilitate clarity of reproduction positive plates are used instead of negative reproductions.

The value of the röntgenogram in helping to establish diagnosis is to a large extent predicated upon the ability to distinguish gas-distended small bowel from colon. The following points have proven of service in distinguishing between the two.

(1) Gas in the small bowel is usually centrally located. The bowel lies horizontally, and may show the so-called pipe organ or ladder pattern, especially if the plate is taken with the patient lying on his back. (Fig. 3.) Frequently, however, the coils may be few and irregularly situated, or there may be only one dilated loop. (Fig. 7.)

Gas in the colon is usually situated peripherally, in the flank. (Figs. 10–13.) The cæcum should always be sought for and will frequently show gas when no other portion of the large bowel can be visualized. With a ptotic transverse colon, gas may, however, occupy the central field. On the other hand, if the plate be taken with the patient on his abdomen, coils of small bowel may be displaced into the lateral colonic fields. (Figs. 1 and 4.)

(2) The colon is characterized by its blunter, deeper indentations due to its haustration. (Fig. 10.) The small intestine has a feathered or ribbed appearance due to its valvulæ conniventes. Its edges have a serrated appearance. These serrations are much more closely placed than the haustrations of the colon. (Fig. 1.)

(3) Gas in the small bowel appears as a homogeneous area of rarefaction in a well-defined loop. In the normal colon discrete spheroid globules of gas are often visualized, perhaps due to entrapment in its saccules.

(4) The fluid levels in the small bowel are centrally placed and have a short vertical height due to its general horizontal course and its numerous turnings. (Figs. 4, 5 and 6.) The large bowel shows fluid levels in the flanks and in the descending and ascending colon which are practically vertical tubes suspended from the flexures; the vertical height of the gas column may reach 4 to 6 inches. (Fig. 11.)

The mode of employment of these röntgenograms in helping to arrive at a diagnosis may perhaps be best illustrated by discussing various types of intra-abdominal small bowel obstruction as they have been encountered clinically. Parenthetically it may be stated that the extent of intestinal distension as shown by the plate is no index to the severity of the underlying condition. We have encountered gangrenous gut with relatively little visualization of loops of small bowel, and on the other hand we have found enormous gas distension in patients with a kinking non-strangulating obstruction.

(1) *Obstructions due to adhesions or bands from an old laparotomy.*—Twenty-one cases. Some of these cases entered the hospital with the diagnosis all too clear. There was a considerable group of them, however, which posed a familiar and difficult problem. The patient is admitted with an abdominal scar, cramps, constipation, nausea, perhaps a little vomiting, and with practically no distension or constitutional symptoms. Naturally, one is loath to operate upon this type of case on the available clinical evidence, and it is in this group in which there is frequently the clinical tendency to "sit

FIG. 5.

FIG. 6.

FIG. 5.—Early case of acute obstruction of the small bowel. Fourteen-hour history. Fluid levels present. In this case no distended loops of small bowel could be visualized on the flat plate. Note absence of gas in lateral colonic fields.

FIG. 6.—Case of tuberculous stricture of the upper ileum with acute obstruction, showing fluid levels and dilated small intestinal loops. Clinically, case was considered one of colonic tumor.

FIG. 7.

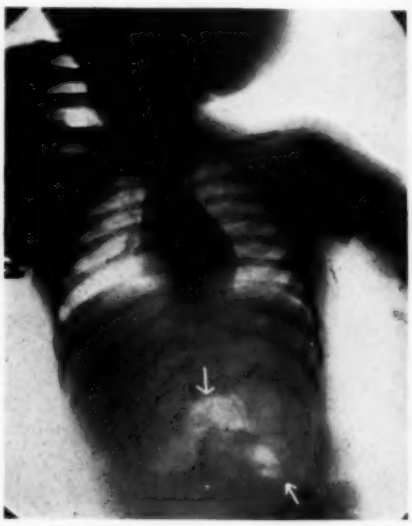

FIG. 8.

FIG. 7.—Unusual distribution of dilated small intestinal loops in a case of obstruction two feet from the ileo-cæcal junction.

FIG. 8.—Case of acute ileo-colic intussusception in an infant. Fluid levels and distended small bowel in a case of ileo-colic intussusception. Note absence of gas in lateral colonic fields.

tight" and await developments, that the X-ray has probably proven of greatest value.

Practically all post-operative acute obstructions due to bands or adhesions occur in the small bowel. Therefore, if dilated loops of small bowel can be visualized with an absence of gas in the colon, a diagnosis of mechanical occlusion can be made. If possible, one should not depend upon the presence of fluid levels alone, for we have seen fluid levels following an attack of renal colic in a patient who had previously been subjected to an appendectomy because of a similar attack. This patient, however, had large quantities of gas in the colon. On the other hand, we have had two cases where fluid levels were found, and in which neither large nor small bowel could be visualized on the flat plate. These patients both had mechanical obstruction.

If gas can be demonstrated in the colon one can be fairly sure that the symptoms are not a result of mechanical obstruction connected with the previous operation. This was borne out in ten cases with previous laparotomy, whose presenting symptoms suggestive of ileus were later shown to be due to such diverse conditions as neuro-syphilis, uræmia, coronary artery disease, poisoning by bootleg alcohol, renal colic, retroperitoneal hæmatoma, low-grade pancreatitis and the lighting up of inflammation in diseased fallopian tubes left behind in a conservative pelvic operation.

In this particular type of obstruction following previous laparotomy, we can say unequivocally that the X-ray frequently gave us more accurate information than the clinical signs. In a number of these cases expulsion of gas had been reported following enemata, and because of the absence of the text-book (or advanced) symptoms of ileus, there was some tendency to favor conservative therapy. In a number of these cases laparotomy, undertaken largely on the strength of the röntgenogram, disclosed definite evidence of mechanical occlusion which could not possibly have been relieved spontaneously. In other words, when the clinical appearances conflicted with the röntgenographical findings, operation proved the latter to be correct.

(2) *Obstruction due to kinking around a colostomy spur.*—Two cases. In one of these patients an abdomino-perineal resection had been performed for carcinoma of the rectum. When signs of obstruction occurred, they were considered by the family physician as due to a colonic obstruction from a recurrence higher up in the colon. X-ray ruled out the possibility of colonic obstruction and demonstrated a small bowel obstruction, which was successfully relieved by operation. In the other case, a colostomy which had been performed for a stenosing proctitis and sigmoiditis underwent considerable narrowing and retraction. The onset of the obstructive symptoms in this patient were at first also attributed to colonic obstruction. X-ray revealed no gas in the colon and dilated loops of small bowel, the findings being verified by operation.

(3) *Obstruction occurring in the immediate post-operative course.*—Four cases. The ileum is the usual site of obstruction in this type of case, and *a priori* it might be assumed that the röntgenogram would be of as much

FIG. 9.

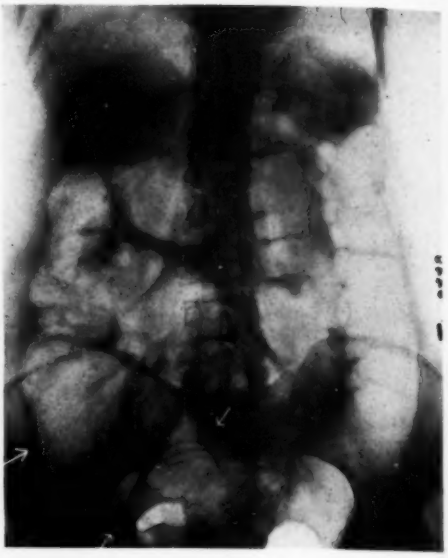

FIG. 10.

FIG. 9.—Strangulated partial enterocele. Dilated loops of small bowel marked by X. Arrows point to gas in colon.

FIG. 10.—Obstruction due to carcinoma of the lower sigmoid. Entire large bowel distended with gas. Cæcum enormously dilated, outlined by arrows. Typical haustration of colon.

FIG. 11.

FIG. 12.

FIG. 11.—Fluid levels in a case of acute obstruction of the lower descending colon by carcinoma. Note the height of the columns of gas on top of the fluid as well as the typical colonic markings.

FIG. 12.—Distension of left and right colon by gas in an acute obstruction due to carcinoma in the mid-sigmoid. Note absence of dilated small bowel in central field.

value as in the previous groups in demonstrating the presence of a mechanical ileus. However, a peculiar type of paralytic ileus unassociated with peritonitis, as well as severe cases of peritonitis, may give the same röntgenological picture as a mechanical obstruction. In a number of cases of paralytic ileus coming to autopsy it was noted that the terminal ileum was collapsed, and that the distension of the bowel increased steadily towards the duodenum. It can readily be understood how this type of ileus could give rise to a röntgenogram simulating a mechanical occlusion. Similarly, severe cases of peritonitis involving the small bowel may produce the same sort of picture.

The X-ray is of value, however, in determining the presence of an obstruction in clean cases where there is no question of peritonitis. In three such cases, one following a herniotomy, another a hysterectomy for fibroids, and the third a clean appendix, it led to immediate operative intervention. The fourth case was a drained appendix in whom the correct differential diagnosis between peritonitis and mechanical occlusion was accidentally made on grounds which we later learned were not certain.

The plain röntgenogram is of considerable value in ruling out the presence of a mechanical ileus. In five cases where the diagnosis of acute obstruction was seriously considered, the presence of gas in the colon dissuaded us from operative intervention. The subsequent course of these cases and an autopsy in one of them proved the correctness of the diagnosis.

To sum up, we feel that in the first week after operation the period during which paralytic ileus and peritonitis are most apt to occur, the diagnosis of mechanical occlusion of the small bowel requiring operative relief cannot be made with certainty by the X-ray. After this period, the presence of fluid levels in the small bowel, dilatation of the small bowel, and absence of gas in the colon may be taken as an evidence of mechanical ileus.

(4) *Obstruction due to spontaneous inflammatory bands.*—In one of these a loop of small bowel was caught underneath a band running towards a chronically diseased appendix. In the other one there was a twist due to an adhesion of a loop of bowel to a segment of omentum which was adherent to a small pro-peritoneal hernia. Both these patients were elderly men in whom the suspicion of colonic obstruction was strong. The röntgenogram successfully localized the obstruction to the small bowel.

(5) *Spontaneous volvulus of the terminal ileum.*—This patient was admitted with a short history, shock and a rigid abdomen. The admission diagnosis was perforated duodenal ulcer. X-rays taken for free air under the diaphragm revealed instead fluid levels in the small bowel. This permitted of more accurate diagnosis and the use of a more advantageously placed incision.

(6) *Tuberculous stricture of the mid-ileum.*—This patient had a history pointing to chronic intestinal obstruction which had suddenly become acute. The suspicion of colonic neoplasm was very strong. Röntgenograms, however, revealed that the obstruction was apparently in the small bowel.

FIG. 13.

FIG. 14.

FIG. 13.—Obstruction in the upper sigmoid by carcinoma with distension mainly present in the cæcum and ascending colon.

FIG. 14.—Typical appearance given by gas-distended sigmoid in a case of sigmoid volvulus. Arrows point to vertex of volvulus.

(7) *Replacement of a gangrenous loop of small bowel by taxis on an irreducible hernia.*—The findings were typical of small bowel obstruction and led to laparotomy which revealed the above findings.

FIG. 15.—An unusual picture in sigmoid volvulus showing both loops, usually only one loop of sigmoid can be visualized.

(8) Obstruction in a knuckle of gut in a small pro-peritoneal hernia in a woman seven months pregnant. Abdominal examination was naturally unsatisfactory and the diagnosis was considerably cleared up by the X-ray which showed dilated loops of small bowel.

(9) Two cases of strangulated partial enterocele (Richter's hernia). One of these occurred in a small femoral hernial sac in a very stout woman; the other in a small hiatus in the sigmoid mesentery. These cases are of unusual interest in that they were both passing small quantities of gas and the X-ray showed small quantities of gas in the colon in addition to dilated loops of small bowel.

(10) *Two cases of intussusception in infancy.*—It is well known that

normally gas can be demonstrated in the small intestine of infants. However, gas is also usually present in the large bowel. In both of the present instances there were fluid levels, absence of gas in the colon, and dilated loops of small bowel.

(11) *Acute obstruction due to kinking of the ileum by an adhesion to a pyosalpinx.*—Two cases. Both these patients had large bilateral masses in the fornices. Inordinate vomiting led to the suspicion of mechanical obstruction and X-ray showed the findings typical of mechanical small bowel obstruction. Numerous control studies on cases of salpingitis and pyosalpinx made on the gynecological service of the Harlem Hospital through the kind coöperation of Doctor Falk, demonstrated that in the distension associated with pelvic inflammatory disease, gas was present either in the large bowel alone, or in both large and small bowel. The only exception noted in adnexal disease was in a diffuse peritonitis due to the rupture of a pus tube into the general peritoneal cavity.

One instance in which we were led astray was in a patient who was admitted to the hospital acutely ill, on the third day of her illness, with tender masses in both fornices. Inordinate vomiting and obstipation again led to the suspicion of mechanical obstruction. The X-ray showed fluid levels, dilated small bowel, and absence of gas in the colon. Laparotomy disclosed a diffuse peritonitis with paralytic ileus from a ruptured gangrenous appendix instead of a mechanical ileus, in addition to a bilateral pyosalpinx.

Paralytic and Reflex Ileus.—These are discussed at the present juncture because of the difficulty that they may offer in differentiation from mechanical small bowel occlusion. Practically this differential diagnosis is encountered mainly in the immediate post-operative phase. Our experiences may briefly be summarized as follows:

(1) *Peritonitis.*—(*a*) In severe cases of peritonitis with pus among the coils of ileum there may be a severe enough paralytic ileus to prevent the intestinal contents from reaching the colon. These patients will show dilated loops of small bowel, fluid levels in the small bowel, and absence of gas in the colon. Of course, röntgenological differentiation from mechanical ileus is impossible. This group is a small one and we have encountered it mainly immediately post-operatively and in cases of *known* peritonitis where control studies were being made. It has been our experience that most of these cases terminated lethally.

(*b*) In peritonitis of lesser severity gas may be demonstrated both in the colon and small bowel. These patients may also have fluid levels in the small bowel. The presence of the gas in the colon is an important factor in ruling out mechanical obstruction of the small bowel.

(*c*) In some types of post-operative distension the peritonitic process is mainly in the flanks, and gas may be present in large quantities only in the large bowel.

(2) *Paralytic ileus without peritonitis.*—In a number of patients coming to post-mortem following the development of symptoms of ileus immediately

post-operatively, the author has noted collapse of the terminal ileum with increasing distension extending orad and becoming quite marked in the jejunum. In one of these cases a mistaken diagnosis of mechanical ileus had been made by the röntgenogram for reasons which can easily be seen.

(3) *Reflex ileus.*—We have seen accumulations of gas in the small bowel and the presence of fluid levels in such diverse conditions as renal colic, obstructed ectopic kidney, retroperitoneal hæmatoma, and pancreatitis. We have also noted them at times following the introduction of ureteral catheters. (We do not wish to convey the impression that these are invariable findings. They are as a matter of fact the *unusual* findings.) The distension of the small bowel in these cases is never as marked as in obstruction or peritonitis and the overlying gas on top of the fluid level are frequently only slit-like. Furthermore, most of these cases also have gas in the colon, which serves to distinguish them from small bowel obstruction. In a number of these cases, as well as in some of the milder types of peritonitis, but never in mechanical ileus, gas could be demonstrated in the colon following an irrigation, when it had been absent previously.

Mechanical obstruction of the Large Bowel.—We consider it of great importance from a practical standpoint to distinguish pre-operatively between colonic and small bowel obstruction. Ileal or jejunal obstruction is either actually or potentially strangulatory and with few exceptions necessitates exploration and relief of the obstruction. Obstruction of the colon, except for the rare cases of sigmoid volvulus, and some types of intussusception, is obturating in nature and is usually on a neoplastic basis. These patients have been suffering as a rule from some degree of partial obstruction before the onset of total occlusion; they are chronically as well as acutely ill. Tension ulcers are frequently present proximal to the obstruction and in our experience the acute shut-down has in a number of instances been precipitated by the œdema around a sealed-off pin-point perforation in the region of the neoplasm. For these reasons, we feel that, by and large, the best results will be obtained in acute colonic obstruction by the performance of a good-sized cecostomy under local anæsthesia through a small incision, leaving the determination of the exact site, nature and operability of the lesion to be decided at some future time when the acute phase has passed off. On the other hand, unless one is absolutely sure that the obstruction is located in the large intestine, there is naturally considerable hesitancy in commencing a cecostomy upon a greatly distended patient through a small incision, poorly placed if exploration should be necessary, and with the unpleasant and dangerous eventuality in intestinal obstruction, of having to resort to general anæsthesia on the table. (The argument might be advanced that these difficulties could be largely obviated by the use of spinal anæsthesia. This is true. However, the induction of spinal anæsthesia by causing contraction and peristalsis of the bowel is to a great extent the equivalent of the administration of a powerful cathartic, and we have observed two cases where we

believe that tension ulcers in the cæcum and transverse colon were caused to perforate in this manner.)

The röntgenogram enables us to diagnose colonic obstruction with complete assurance. (Fig. 10 *et seq.*) The outlines of the distended colon proximal to the obstruction and the presence of fluid levels in it are unmistakable. (Figs. 11-15.) The site of the obstructive neoplasm was in the sigmoid in 12 instances. In 11 of these cases the entire large bowel was distended with gas and could be seen with unmistakable clarity. In the other case the distension was for some reason mainly localized to the cæcum and ascending colon. The splenic flexure, the transverse colon and the hepatic flexure were each the site of obstruction on one occasion. The obstruction was correctly localized in each instance by the flat plate. In the patient with the obstruction at the hepatic flexure, it was further verified by a barium enema and an ileo-transverse colostomy instead of a cecostomy was performed (the only time in this series) in order to leave a clean field for the secondary right-sided resection.

It is interesting to note that even in cases of long-standing obstruction of the colon, dilated small bowel or fluid levels in the small bowel, are not as a rule visualized. Another point worth mentioning is that in some cases of very prolonged obstruction there may be little gaseous distension. Thus in a case seen at another institution, and not included in this series, a patient who had been completely obstructed for two weeks from a tumor in the descending colon showed very little gaseous distension in the colon, but had a foamy appearance throughout the course of the large bowel, probably due to mixture of gas with semi-solid stool. At operation the colon was found to contain putty-like fæces.

Volvulus of the sigmoid was encountered five times in this series, an unusually high percentage. A definite diagnosis of volvulus of the sigmoid was made in four instances. In the other instance the diagnosis was simply that of obstruction of the large bowel. The plate in this instance was a poor one. The sigmoid is a relatively non-sacculated and non-haustrated portion of the colon, a fact which serves to distinguish it from other parts of the large bowel. When volvulus occurs the distension is practically limited to the twisted sigmoid loop. It achieves a distension much too enormous for small gut and can be seen to occupy a large portion of the abdominal cavity as a single well-defined loop. In one instance, both loops of the volvulus could be visualized as well as the base of the inverted U formed by the twisted gut. In the other cases only one of the limbs and the base of the U could be visualized.

CONCLUSIONS

(1) The plain röntgenogram of the abdomen without the use of contrast media is a distinct aid to the diagnosis of acute mechanical intestinal obstruction.

(2) It may be a decisive factor favoring operation in cases clinically doubtful.

(3) It may prevent exploratory laparotomy in patients with signs suggestive of ileus.

(4) It permits differentiation between large and small bowel obstruction.

(5) The cardinal signs of small bowel obstruction are: (*a*) Visualization of dilated loops of small bowel. (*b*) The presence of fluid levels in the small bowel. (*c*) Failure to visualize gas in the colon.

(6) Patients with symptoms of ileus in whom gas can be demonstrated in the colon are probably not suffering from mechanical occlusion of the small bowel.

(7) In the immediate post-operative phase caution must be used in differentiating mechanical obstruction from paralytic ileus or peritonitis, as all of these may give the same X-ray picture.

(8) The presence of fluid levels in the small bowel alone is not pathognomonic of mechanical obstruction. They have been encountered in peritonitis, in paralytic ileus, and in reflex ileus.

(9) Fluid levels and dilated loops of small bowel are probably not due to mechanical obstruction if there is coincident presence of gas in the colon.

(10) To reduce the chances of error it is advisable to take plates in the recumbent and erect positions.

(11) The diagnosis of colonic obstruction is easily made due to the marked distension of the colon proximal to the site of obstruction, and the presence of fluid levels with high vertical gas columns in it.

(12) Distended small bowel is not as a rule visualized in colonic obstruction.

(13) Localization of the obstruction in the colon is possible in a rough fashion. If necessary a barium enema may be used to confirm exact localization.

(14) Sigmoid volvulus can usually be diagnosed as such from X-ray appearance.

The author wishes to thank Dr. John F. Connors, Director of the Surgical Service at Harlem Hospital, for his permission to report the cases on his service. He is also indebted to Dr. A. A. Berg, Dr. Edwin Beer, Dr. Richard Lewisohn and Dr. Harold Neuhof in permitting him to study the cases admitted to their respective services at the Mt. Sinai Hospital. To Doctor Jaches, of the Mt. Sinai Department of Radiology, and Doctor Snow of the Harlem Hospital, he is indebted for numerous courtesies.

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CARCINOMA OF THE HEPATIC DUCT

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Schneppel is credited with being the first to describe carcinoma of the hepatic duct in 1878. Since then occasional reports of carcinoma of the biliary ducts have appeared in the literature. Rolleston's group of ninety-one cases is the largest and shows well the incidence in the different parts of the biliary duct system, excluding carcinoma of the ampulla and gall-bladder.

Common duct:	
Lower end	23
Middle	11
Junction, hepatic, common and cystic ducts	28
Common hepatic	19
Right or left hepatic	4
Cystic duct:	
Lower common duct	6

A number of interesting reports of carcinoma of the hepatic duct have been made. It has been pointed out (Kauffman) that the carcinoma may occasionally be villous or diffuse in character but that usually the growth is nodular and encircles the duct and converts it into a thick tube over a distance of one to two centimetres of its length. The size of the tumor varies from a pea-sized nodule to a swelling the size of a small hen's egg. Cases have been reported where the gastrohepatic ligament, pancreas, liver, portal vein or retroperitoneal glands have been involved but in the great majority of cases the growth is local and no evidence of metastases exists. Devic and Galfavardin found metastases in 20 per cent. of the cases they reviewed. Unlike carcinoma of the gall-bladder, gall-stones are found in only one-third of the cases. Histologically the tumor is composed of columnar cells, usually sparse in number, which are found embedded in great masses of fibrous connective tissue. It is the object of this communication:

(1) To call attention to the great similarity of the clinical course of carcinoma of the hepatic duct to common-duct stone where repeated severe colics, intermittency of the jaundice, non-dilated gall-bladder and chronicity of the course of the disease are characteristic.

(2) To emphasize the fact that at the operation the findings resemble but remotely those of common-duct stone and are characteristic of carcinoma of the hepatic duct in that the common duct and gall-bladder are normal, whereas the hepatic duct is converted into a firm, fibrous cord resembling in every way dense scar tissue. Unless this fact is known the diagnosis at operation is likely to be missed.

(3) To emphasize that when the stricture of the hepatic duct from carcinoma cannot be removed by operation and therefore jaundice continues that post-operative hæmorrhage is likely to occur and may be a fatal termination.

The report of the following two cases brings out these points:

Case I.—I. H., male, sixty-eight years of age, seen with Doctors Billings, Post, and Thomas, entered the Presbyterian Hospital December 8, 1929; died December 17, 1929.

Present complaint.—For the past four days patient has had pain in right upper quadrant, dull in character, coming on after meals and often continuing all night. Deep jaundice has been present for three days and diarrhœa has been present for seven days. Stools are white. There has been no nausea or vomiting.

Past history.—One year ago patient had acute indigestion so severe that he fainted from the pain.

Examination.—Rather heavy man with negative physical findings except deep jaundice and acholic stools; liver rather firm and three fingers below the costal arch; gall-bladder not palpable. Fluoroscopic examination of stomach and bowel is negative. The flat X-ray plate of gall-bladder region shows several large stones.

Diagnosis.—Obstructive jaundice, gall-stones and probable common-duct stone.

Operation.—December 9, 1929, under ethylene-gas-ether anæsthesia. A right para-rectus incision was made and a thick gall-bladder was encountered containing many stones and one large stone the size of a pigeon's egg which could not be dislodged from cystic duct. The gall-bladder was opened and split down to the cystic duct and the stone removed. It was then found that the hepatic duct was converted into a hard, fibrous mass reaching from the liver parenchyma downward for about 1½ centimetres. The common duct was not dilated. The pancreas and stomach were normal. The incision was continued downward through the cystic duct into the common duct because of difficulty of bringing the common duct into the wound. There was practically no bile present in the common duct. A probe inserted upward through the common duct met firm obstruction in the hepatic duct. It was thought that the mass was scar tissue and produced by long-standing inflammation extending from the gall-bladder, which lay directly contiguous to it. After several minutes' examination with a probe a very small lumen was found in the hepatic duct and this was gently dilated by small forceps until a small catheter could be inserted through the stricture, where it was sutured into place. To our surprise but little bile was obtained and at no time after operation were there more than a few cubic centimetres of bile discharged. The gall-bladder was removed and the wound closed with cigarette drainage. Oozing of fresh blood from the wound began on the fifth day and persisted in spite of calcium administration and glucose by hypodermoclysis. On the sixth day 350 cubic centimetres of blood were transfused by the direct method. The wound was opened and packed. Five hundred cubic centimetres of blood were given by transfusion on the ninth day post-operatively without effect. In the evening of the ninth post-operative day the patient died.

The autopsy revealed a tubular constriction about 1½ centimetres long, beginning at the junction of the right and left hepatic ducts. Above the obstruction the intra-hepatic ducts were widely dilated but contained little bile. There was slight extension of the carcinoma in the hepatic duct into the gastrohepatic ligament. No other evidence of extension of the growth or metastases was found. The intestinal tract contained a large amount of blood and there was a hæmorrhagic infarction of the duodenum.

Histologically, the lesion of the hepatic duct was a columnar cell scirrhous carcinoma. (Fig. 1.)

Case II.—A. H., female, aged thirty-one. Entered the Presbyterian Hospital March, 1928, on the service of Dr. R. T. Woodyatt. She complained that since January, 1928, she had had three attacks of severe upper abdominal pain, radiating to the back under the right scapula. She vomited during the attacks. Hypodermics were necessary

to control the pain. During the attacks she thought that she became slightly jaundiced. On examination there were no unusual physical findings. The Wassermann was negative. No abdominal tenderness. Ten tablets of Iodekon gave no filling of the gall-bladder with dye. In June, 1928, she returned to the hospital with a history of repeated attacks of pain and jaundice after the attacks. The jaundice cleared between the attacks. She was tender and rigid over the right upper quadrant of the abdomen, white blood cells 16,300, red blood cells 3,930,000.

In July, 1928, she was operated upon in another city at which time the gall-bladder, which contained no stones, was removed. The common duct was opened without finding any stones or other pathology and was drained. After the operation she was greatly relieved and had no jaundice for about six months. At that time she had another attack with severe pain accompanied by jaundice. She became rather weak and nervous

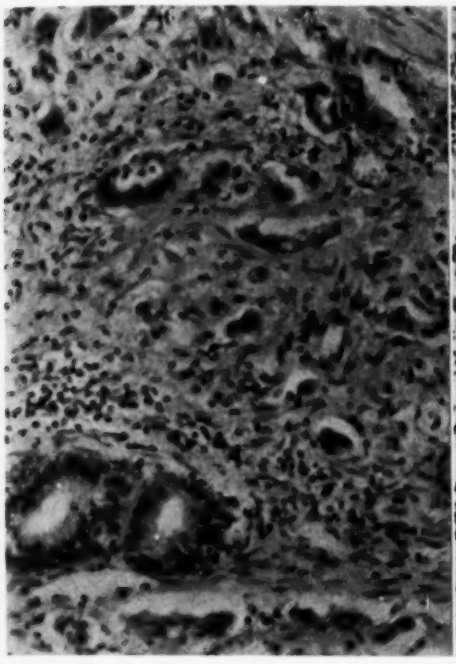

FIG. 1.—Case I. Scirrhous adenocarcinoma of the hepatic duct.

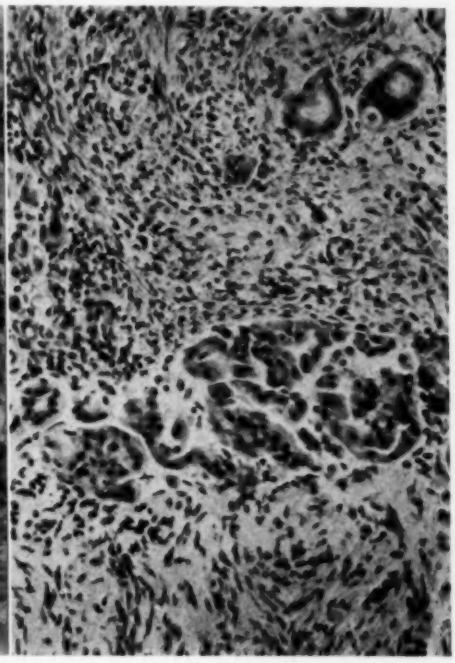

FIG. 2.—Case II. Scirrhous adenocarcinoma of the hepatic duct.

and developed tremor. On examination the liver margin was sharp. There were no intra-abdominal masses palpable. The basal metabolic rate was minus 11.

December, 1930, she returned to the Presbyterian Hospital with the complaint that she had severe pain in the region of the gall-bladder, lasting for three or four hours at a time. Just before Christmas, 1930, her jaundice cleared up, but in January, 1931, jaundice returned and she had a dull pain in the upper abdomen. She had no chills. Her stools had become clay colored and the icterus index rose from plus 16 to plus 45.

With the diagnosis of probable common-duct stone we advised reoperation and upon February 7, 1931, the old scar was removed, but great difficulty was encountered in getting into the peritoneum because of dense, fibrous adhesions obliterating the upper peritoneal cavity. The liver was densely adherent to the anterior abdominal wall. The upper abdominal contents were separated from the liver downward, the common duct was identified and when opened was found normal in size and a probe passed easily into the duodenum. The common duct, however, contained no bile. The probe passed

upward encountered an obstruction in the hepatic duct which was found to be due to a firm, fibrous thickening about the size of the terminal phalanx of the thumb, including the whole circumference of the duct. This mass was needled in many directions thinking that a stone might be found in the centre of the firm mass in the hepatic duct. No stone, however, was encountered. A small piece of the mass was removed for section and a diagnosis of carcinoma of the hepatic duct was made because of the similarity of the findings to those described in Case I. There were no enlarged glands, the liver was small and dark-green and contained no palpable metastases. A "T" tube was sutured into the common duct.

The second day after operation bile drained intermittently through the tube for several days. On the fifth day after operation there was marked oozing from the abdominal wall which continued for about a week. The patient remained deeply jaundiced, became weaker and died March 18, about five weeks after the operation.

The histological examination of the biopsy material showed dense scar tissue containing here and there small groups of epithelial cells. Our pathologist would not commit himself on the diagnosis though by physical findings at operation I felt confident that the mass was a carcinoma of the hepatic duct.

At autopsy the following pathological conditions were revealed: Scirrhous adenocarcinoma of the hepatic duct—no glandular metastases. Dilatation of the intrahepatic ducts. Suppurative cholangitis. Obstructive biliary cirrhosis. Marked emaciation. Extreme jaundice. Acute left pyelitis and acute cystitis. Encapsulated large nodule of tuberculosis in left lung. Small ovarian cyst. Patent foramen ovale.

THE PREDICTION OF HÆMORRHAGE IN OBSTRUCTIVE JAUNDICE BY THE SEDIMENTATION RATE

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It has long been recognized that patients with obstructive jaundice frequently tend to bleed either from wounds made during operation for the relief of their obstruction or spontaneously in the absence of any recognized trauma. This hæmorrhagic tendency has interested clinicians and laboratory investigators for many years, first because it renders any operative procedures on these patients extremely dangerous, second, because measures to prevent its occurrence, though long investigated, are inadequate in certain cases, and, finally, because there has been no positive way by which with laboratory tests or clinical examinations this tendency to bleed could be foretold.

Dr. Robert R. Linton,[1] in 1930, reported his opinion that the sedimentation rate of the red blood-cells could be used as an index of the hæmorrhagic tendency in obstructive jaundice. It is of particular clinical value in obstructive jaundice to know before operation is undertaken whether or not the patient will bleed. If, then, a simple test—the sedimentation rate of the red blood-cells—can be depended upon to give us this information, it will be of great advantage. After reading Linton's article, we have used this test in every patient with obstructive jaundice, both before and after operation, and it is our desire to present the results of these experiences at this time.

Opinions as to the cause of bleeding in obstructive jaundice differ widely. Wangensteen[2] has given a most comprehensive review of the literature upon this subject and in our opinion his deductions are logical. His article may be read with profit by anyone interested in this subject. Numerous factors have been considered as the cause of the hæmorrhagic tendency in jaundice; *i.e.*, the presence of the bile pigments and the bile acids in the blood-stream; a functional deficiency of calcium due to the increase in bile salts and bile acids in the urine and in the blood; and variation in the prothrombin and fibrinogen contents of the blood. None of these factors, however, can be proved experimentally as the sole cause of this tendency. It is probable, Wangensteen states, that normal coagulation of the blood is related to normal hepatic function and any destruction of liver tissue, combined with loss of function of the liver, directly alters the coagulation ability of the blood. It has been shown repeatedly that marked damage of liver structure results in failure of the blood to clot and it is known experimentally that extracts of liver tissue prevent the clotting of blood. It seems logical, therefore, to

assume that the chief factor in the tendency to bleed in obstructive jaundice is the presence in the blood-stream of products arising from the actual destruction of liver tissue and failure of liver function.

It is a fact that until Linton proposed the sedimentation rate there was no laboratory test which was a reliable index of the tendency to bleed in obstructive jaundice. It is common knowledge that estimation of the coagulation time of the blood and of the bleeding time are of no value in predicting the tendency to bleed. Thus in five of our cases the coagulation time and bleeding time were normal and yet serious hæmorrhage occurred. Conversely, in other cases the coagulation and bleeding time were prolonged and no hæmorrhage occurred. Lewisohn[3] made a study of the blood-clotting factors in obstructive jaundice as proposed by Bancroft, Kugelmass and Stanley-Brown[14] as an index of the tendency to bleed. For this purpose they estimate the prothrombin, the antithrombin and the fibrinogen of the blood and obtain a clotting index. The index is obtained by multiplying the prothrombin with fibrinogen and dividing it by the antithrombin. They state that if the index is .7 or above, the prognosis as to hæmorrhage is good, and when it is below .7 the tendency to hæmorrhage is definite. We have had no experience with this clotting index in jaundiced patients. It is an elaborate procedure, technically difficult and not readily performed. It has not as yet been done in a sufficiently large number of cases to warrant any conclusion.

Linton states that the sedimentation rate of the red blood-cells is apparently rapid in those patients with obstructive jaundice who tend to bleed and it is low or normal in those patients with no tendency to bleed. In the first studies of this reaction he reported seven cases of obstructive jaundice in which the sedimentation rate was rapid who had post-operative bleeding and ten other cases with normal slow rates who had no post-operative bleeding. It is desirable that further experiences, such as ours, shall be reported. If this relationship between the rapidity of the settling of the red blood-cells and the tendency to bleed is positive, the test is of very definite clinical value, since it has the great advantages of being simple to perform and inexpensive to do repeatedly.

It is well recognized that any one of innumerable factors may influence the sedimentation rate. Serious infection, fever, extensive malignancy, pregnancy, anæmia, exercise—all may effect the rapidity of settling of the red blood-cells. The possible presence of these factors in interpreting the tests must be considered. Our experience, however, has shown that fever is the chief complicating factor which one commonly encounters in obstructive jaundice that may affect the sedimentation rate. We, therefore, try to take the blood for sedimentation rate only in afebrile periods and to discount sedimentation rates taken when the patient had fever of marked degree.

The technic used in the laboratories of the New England Baptist Hospital and the New England Deaconess Hospital is that recommended by Plass and Rourke,[4] as recorded by Linton, with certain slight modifications suggested by Miss Hazel Hunt, of the Deaconess Laboratory.

The sedimentation tubes are specially prepared graduated glass tubes. (Fig. 1.) They hold from 1.11 to 1.18 cubic centimetres of blood and are

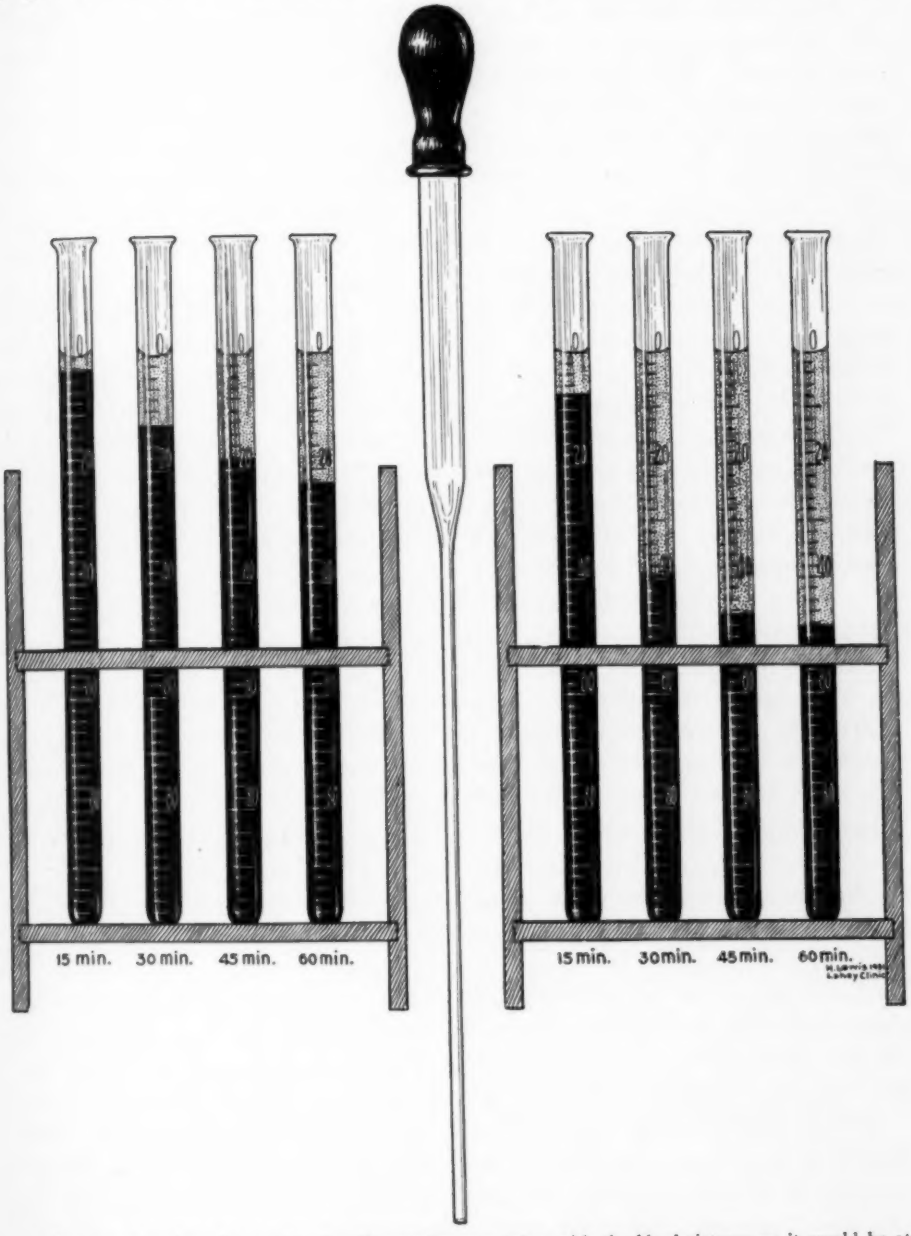

FIG. 1.—Drawing of two sets of sedimentation rate tubes with the blood-pictures as it would be at the varying intervals following the start of the test. On the left is seen the picture of the normal sedimentation of the red cells in a sixty-minute test. On the right is the sedimentation rate as seen when it is rapid. In the centre is the long thin pipette, devised by Miss Hunt for filling the sedimentation tube with blood and avoiding the presence of bubbles or air pockets.

graduated from zero at the top to one hundred at the bottom in millimetres. In their original work Plass and Rourke used calcium oxylate to prevent the

coagulation of the blood. Later they recommended the use of heparin. In this work potassium oxylate has been used.

Four cubic centimetres of venous blood are collected in the usual manner from a vein in the patient's arm and mixed with twenty milligrams of potassium oxylate. At the suggestion of Miss Hunt a long capillary pipette is used to transfer this blood to the sedimentation tube. The pipette reaches the bottom of the tube and from this point the filling of the tube is carried out. By this means the entrance of air bubbles and uneven filling is prevented. The tube is then placed in a test-tube rack and readings of the amount of the settling of the red blood-cells in millimetres are made directly from the tube every fifteen minutes for one hour.

Linton arbitrarily adopted the reading at the end of thirty minutes as the desirable reading from which to draw his conclusions of the rapidity of the sedimentation process. In a normal individual the red blood-cells tend to settle slowly and thirty millimetres may be considered the normal high point for the settling of these cells after a thirty-minute interval. (Fig. 1.) If the cells have settled more than thirty millimetres in thirty minutes the sedimentation rate may be considered rapid and if they have settled less than thirty millimetres in thirty minutes the sedimentation rate may be considered slow or normal. From our experience we believe that forty millimetres may be taken as the limit of normal sedimentation in jaundiced patients, which is somewhat higher than the figure recommended by Linton.

We have studied twenty-six cases of obstructive jaundice due either to stones in the common duct, malignancy involving the common duct or stricture of the common duct in relation to the effect of the jaundice on sedimentation rates. On careful analysis of these twenty-six cases, we have found that there are insufficient data on eight patients to warrant any conclusions being drawn. This leaves us, therefore, with eighteen patients in whom we consider we have sufficient information to warrant deductions.

In seven of the eighteen patients the sedimentation rate was rapid, rising in each instance to fifty or above in thirty minutes. In six of these seven cases bleeding occurred and in one no bleeding was noted.

In eleven of the patients the sedimentation rate was either low or only slightly elevated above thirty. In ten of these cases no bleeding occurred. In one, slight oozing from the incision, from the common duct, from the bladder and from the alimentary tract was present for three days.

From the above it is at once evident that the sedimentation rate is not an absolutely positive test for the tendency to bleed in obstructive jaundice since bleeding occurred once when the rate was slow and failed to occur in one case when the rate was rapid. It is desirable to consider particularly the two exceptions to Linton's findings. In one case, No. 24532, the rate became rapid post-operatively yet no bleeding occurred. This patient had obstructive jaundice and also a severe cholangiitis due to a duodenal ulcer involving the pancreas and common duct. Whether jaundice arising from hepatic infection produces a different effect on the sedimentation rate than simple obstructive

jaundice is not known. This patient had from one to two degrees of fever when his rate was rapid but we have not previously seen as marked an increase of sedimentation rate with such slight elevation of temperature.

The second case, No. 10,326, in this series in which the sedimentation rate did not accurately predict the tendency to bleed was the converse of the one just stated. This patient had severe jaundice due to a large common-duct stone and also an infectious cholangitis. Her jaundice persisted for many weeks after the obstruction was removed. Her sedimentation rate on admission was slow but before operation it was 46. Post-operative bleeding was predicted and therefore she was transfused the day before operation and the day of operation with whole blood. Following operation the rate fell to a low figure and remained at this level. On the sixth post-operative day, however, slight oozing occurred from the wound and blood was passed in the urine and by coughing. A third whole blood transfusion was given which controlled the bleeding at once. No further hæmorrhage has occurred in spite of jaundice persisting for several weeks after operation. The sedimentation rate has remained slow all this time. This patient must doubtless be considered an exception to the rule yet one must note that her rate was rapid before operation and from this bleeding was predicted. The bleeding, however, occurred six days after two transfusions and in the presence of a slow sedimentation rate repeatedly and carefully checked.

The chart in Fig. 2 shows the sedimentation rates of the seven patients who bled following operation for their obstructive jaundice. On the chart are noted the sedimentation rate, the days of operation, the time of bleeding, and the results following transfusion of either citrated blood or whole blood. The first patient who bled, No. 11,902, had a hopeless stricture of the common hepatic duct with serious jaundice of long duration. It is important to note that her bleeding and coagulation time were normal, that her sedimentation rate rose rapidly after operation and that bleeding occurred soon after operation. One may note that with whole blood transfusion the sedimentation rate dropped somewhat but soon rose again and at the same time more serious bleeding arose which finally was the cause of a fatal result. This patient had been jaundiced for many months and her condition was considered a hopeless one because of the location of the stricture.

The second case on the chart, No. 23,075, had normal bleeding and coagulation time on entrance to the hospital. The sedimentation rate at the time of operation was moderately increased and therefore a citrate blood transfusion was done after the operation. Post-operatively bleeding occurred and at this time the sedimentation rate was noted to be sixty-two, which is definitely rapid. A whole blood transfusion was now given and immediately following this the bleeding ceased. Within three days the sedimentation rate fell rapidly and no further bleeding occurred.

In the third case, No. 23,529, we had another hopeless stricture of the common duct with jaundice of long duration. Here, again, the bleeding time and coagulation time were normal on admittance to the hospital, but the sedimentation rate was rapid at the time of the operation. A whole blood transfusion was given and the sedimentation rate came down. On the fifth day after operation bleeding occurred. It is to be noted that the sedimentation rate had risen constantly and was 54 at the time of bleeding. Here, again, whole blood transfusion was given with some improvement which was, however, only transient. The sedimentation rate continued to be rapid, bleeding persisted and was not checked by two more citrate blood transfusions. The patient died ten days after opera-

tion. It is of interest to note here that at the height of the bleeding, with a rapid sedimentation rate, the coagulation time and bleeding time were again taken and found to be normal.

In case No. 20,632 the sedimentation rate was 40, which is definitely rapid at the time of operation. Transfusion here was done following operation and in spite of this the sedimentation rate rose to 50 and hæmorrhage occurred. Two transfusions of whole blood were then performed at three-day intervals, the bleeding stopped and the sedimentation rate dropped to 10. Ten days after the last transfusion bleeding again occurred and at this time the sedimentation rate was rapid. Transfusion was used to check the bleeding and coincidentally the sedimentation rate became slow. The patient had no further bleeding during her convalescence. It is to be noted in this chart that the sedimentation rate rose a few days after her last hæmorrhage, when a subphrenic abscess developed. By this time, however, the jaundice had entirely cleared and no further complications relating to bleeding were present. With drainage of the subphrenic abscess the patient made a most satisfactory convalesence.

In case No. 23,333 there is a marked drop in the sedimentation rate in the three-day interval spent in the hospital before operation from 42 to 24. At operation a whole blood transfusion was given and no immediate post-operative bleeding occurred. On the fifth day, however, a small amount of bleeding was noted in the wound and at this time, furthermore, the sedimentation rate was very definitely elevated to 62. Because the bleeding was so slight, transfusion was not done immediately but the patient was given increased fluids and glucose by veins and subpectorally. With twenty-four hours the ooze from his wound stopped and the patient made an uneventful convalescence. Coincident with the cessation of bleeding the sedimentation rate fell to 28.

In case No. 60,715 serious bleeding occurred and was undoubtedly one of the chief factors causing a fatal result. This patient had an obstructive jaundice proven at autopsy to be due to a high stricture at the junction of the right and left hepatic ducts. At operation a gall-bladder full of stones was removed; the common duct was small and thin-walled. It was explored. No stones were present and the stricture was not discovered. After operation the jaundice persisted and deepened and death occurred fourteen days later. The sedimentation rate correctly predicted the hæmorrhagic tendency in this case as is seen on the chart. It rose rapidly following operation and coincidentally hæmorrhage occurred.

In these patients who bled we have been increasingly impressed with the necessity of whole blood transfusions to control the bleeding. Citrate transfusions were used three times for the control of hæmorrhage in these patients and in none of these instances did the hæmorrhage stop after this treatment. On the other hand, nine whole blood transfusions were used in this group of patients and in no instance did this fail to control the bleeding for an appreciable time. We feel, therefore, from our recent experience, that whole blood transfusions rather than citrate transfusions should be used in the preparation of patients for operation with a tendency to bleed and in the treatment of hæmorrhage following operation in obstructive jaundice.

Eleven patients in this series had no hæmorrhage following the relief of their obstructive jaundice. Their charts with the daily sedimentation rates and the times of operation are shown herewith. (Fig. 3.) The sedimentation rate in six of these patients was elevated somewhat above 30 at the time of operation, yet in none of these patients did even the slightest bleeding occur.

Case No. 23,832, a cancer of the gall-bladder involving the cystic and common ducts, had a rapid rate on admission which was still rapid in spite of pre-operative treatment with fluid and glucose at the time of operation. Following operation he was transfused with whole blood. Within a few days the rate returned to normal and at no time did any bleeding occur.

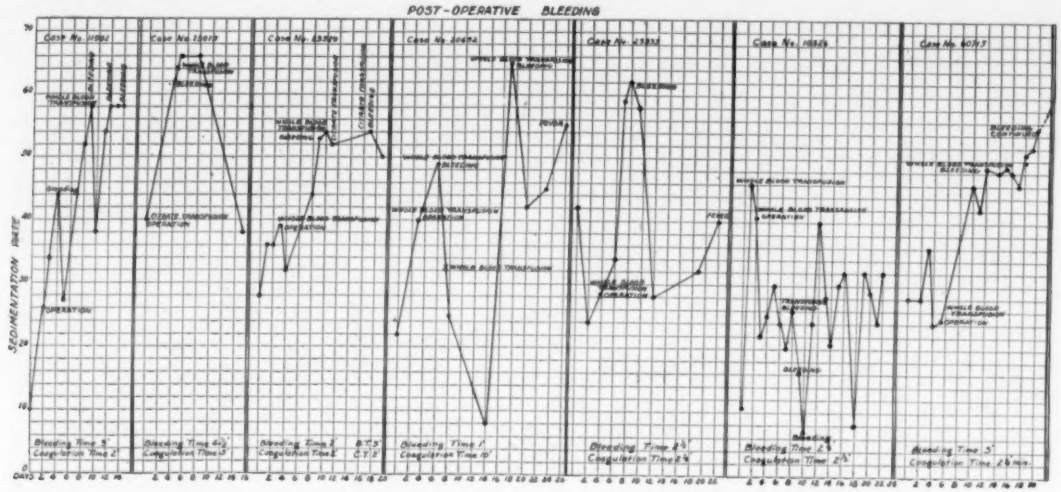

FIG. 2.—Chart showing the sedimentation rates, time of operation, transfusions of blood, either whole or citrate, and the time of bleeding, in the seven cases who bled after operation. Note that the sedimentation rate is rapid in all of these save one—Case 10,326, a patient with common-duct stones and fatal cholangiitis.

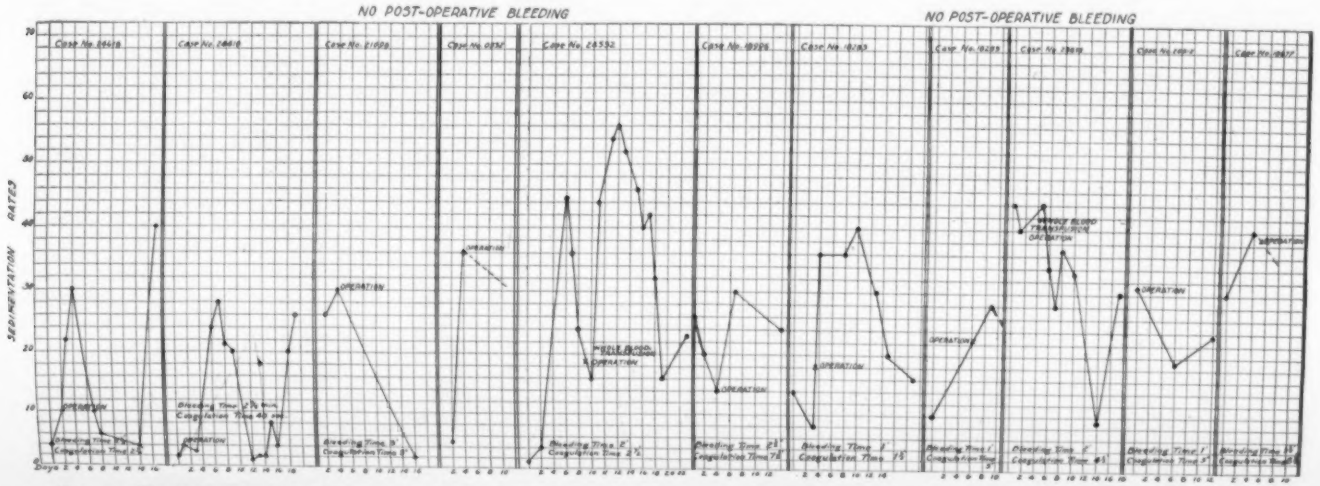

FIG. 3.—The sedimentation rate, time of operation and treatment in eleven patients in whom no post-operative bleeding occurred. Note that the sedimentation rate was relatively slow in all these patients save one—Case 24,532, a patient with a duodenal ulcer and cholangitis on whom a cholecystgastrostomy was done.

We may summarize our experience with the sedimentation rate as an index of the tendency to bleed in obstructive jaundice as follows. In eighteen patients with obstructive jaundice bleeding occurred seven times and no bleeding occurred eleven times. Nine of the patients had sedimentation rates which were above 40 but only seven were persistently elevated above this level. Of the seven patients who had definitely accelerated rates six bled and one did not. In those patients in whom the rate was low, ten had no bleeding and one patient bled.

It is of interest to note that the exceptions in each group who failed to follow the course predicted by Linton had, in addition to the obstruction of the common duct, an infectious jaundice of severe degree. Thus in the one low sedimentation rate case who bled, infectious jaundice was a prominent feature for many weeks. In the one patient with rapid sedimentation rate who did not bleed, infectious jaundice was a large part of the post-operative difficulty. We do not feel that these cases can be excluded, however, from the group under consideration since they had definitely obstructed common ducts in addition to their cholangiitis. If the test is not sufficiently inclusive to permit us to predict bleeding in patients who have cholangiitis in addition to obstruction, this factor must be considered in the interpretation of the test in each case.

For some time in our early study of this test we felt a considerable confidence that a rapid rate meant hæmorrhage would surely occur and a slow rate meant no bleeding would occur. More recently, however, as our experience has increased and our number of cases has grown, we have been greatly disappointed to find definite exceptions to the above prediction. We feel, therefore, that, although the test is very suggestive, much more study and experience are necessary before any final conclusions can be drawn. At present we do not believe that the sedimentation rate can be taken as positive evidence of the tendency to bleed in obstructive jaundice. Our experience would warrant the assumption that in all probability the rate will suggest the post-operative tendency, but that it cannot be depended upon as an absolute criterion. In spite of this fact we feel this test is of definite clinical help in predicting hæmorrhage in obstructive jaundice.

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THE RELATION OF THE BLOOD FIBRIN TO THE HÆMORRHAGIC DIATHESIS OF OBSTRUCTIVE JAUNDICE

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The hæmorrhagic tendency in patients with obstructive jaundice has long been recognized. As yet there has been no adequate explanation of the cause of this predisposition to hæmorrhage. It is not known whether some factors necessary in the coagulation of the blood are deficient, or whether there is an increase in some of the anti-coagulants normally circulating in the blood.

For a number of years the blood calcium was thought to be deficient, or to exist in a form unavailable for the clotting of the blood. Recent investigations,[1, 2] however, have thrown much doubt on this theory. A number of investigators have shown there is no deficiency, either qualitatively or quantitatively, in the blood calcium. Other theories of the cause of the bleeding tendency such as an accumulation of bile-salts or bile-pigments have also been disproven.[3, 4, 22]

At the present time none of the methods in use to prevent or correct the hæmorrhagic tendency, by the administration of drugs, is grounded on sound scientific basis. The most effective means of control is the repeated transfusion of whole blood. In some cases even this fails and the patient dies from uncontrollable hæmorrhage. Whether it is the addition of normal platelets, or other elements necessary for coagulation, which controls the bleeding in some of the cases, is not known. The various methods, including the use of calcium chloride intravenously, have proven inadequate in a great many cases.[2] Attempts to improve the liver function by means of a high carbohydrate and fluid intake are of importance both pre-operatively and post-operatively, but if hæmorrhage has commenced these measures are of little immediate value.

The Blood Fibrin in Severe Liver Disease.—The blood fibrin is one of the important elements in the coagulation of the blood. The chief and perhaps sole source of it is the liver. In the hæmorrhagic diatheses associated with severe liver destruction, produced experimentally by phosphorus or chloroform poisoning, there is a marked diminution of the blood fibrin. This decrease is thought to explain the diminished coagulability of the blood in marked parenchymal liver damage. In obstructive jaundice of long standing there has been shown to be considerable parenchymal liver damage.[11, 12] Because of these facts, I have investigated the blood fibrin in a group of patients with obstructive jaundice, to see if a diminution in this substance may play a rôle in the associated hæmorrhagic diathesis.

According to Melchior,[19] Wunderlich, about seventy-five years ago, noted bleeding in cases of phosphorus poisoning, cholangitis, carcinoma of the liver parenchyma and in

jaundice, and it is reported that he found a decrease of the fibrin in these cases. In 1894 Corin and Ansiaux,[6] working with phosphorus poisoning, concluded that the incoagulability of the blood was due to a decrease in the fibrin. In 1900 Jacoby[18] corroborated this work. Later in 1905 Doyon[7] and his co-workers showed that there was a similar decrease of the fibrin and an associated incoagulability of the blood, in chloroform poisoning. They thought this reduction of the fibrin in both phosphorus and chloroform poisoning was due to a toxic action on the liver.

In 1911 Whipple and Hurwitz[8] confirmed the work of Doyon on chloroform poisoning. Later in 1921 Foster and Whipple,[9] continuing the work, also found a decrease of the fibrin following severe liver damage and associated with this, a marked incoagulability of the blood. They also noted that the fibrin returned to normal as hepatic repair occurred. Schultz *et al.*[10] recently confirmed this hæmorrhagic diathesis in severe liver damage, which is apparently explainable by the diminished blood fibrin.

Normal Blood Fibrin.—The normal blood fibrin level varies considerably according to the figures reported in the literature. Foster[14] states that variations of approximately 15 per cent. above or below the average are to be considered within normal limits. The normal fibrin values for humans are given in Table I. These four sets of figures seem to be the most reliable that have been reported in the literature. The average number of milligrams of fibrin per 100 cubic centimetres of blood and plasma, according to the above set of figures, vary respectively from 155 to 172 and from 280 to 338. The mean values are 166 milligrams of fibrin per 100 cubic centimetres of blood and 321 milligrams per 100 cubic centimetres of plasma.

TABLE I

Normal Fibrin Values (Human)

Investigator		Fibrin per 100 cc. Plasma	Fibrin per 100 cc. Blood
Gram,[13] 50 determinations	Maximum	370	200
	Minimum	205	115
	Average	280	155
Foster,[14] 42 determinations	Maximum	457	221
	Minimum	256	127
	Average	338	171
McLester,[15] 15 determinations	Maximum	385	...
	Minimum	272	...
	Average	333	...
Foster, and Whipple,[14] 4 determinations	Maximum	364	178
	Minimum	316	163
	Average	335	172

Blood Fibrin in Obstructive Jaundice.—Blood-fibrin values in obstructive jaundice have been reported by several investigators. These have been isolated determinations in the majority of instances.

Whipple, and Hurwitz[8] in 1911 noted in a dog with complete obstruction of the common bile-duct there was a slight elevation of the blood fibrin at the end of two weeks. Gram[13] in 1922 reported seven blood and plasma fibrin determinations in four cases of obstructive jaundice due to carcinoma of the pancreas and bile-ducts. All of

these figures are several times the normal value, but he did not mention the incidence of hæmorrhage. Foster[14] in 1924 reported the blood- and plasma-fibrin values in two cases of obstructive jaundice. In both cases the values are above normal. McLester and co-workers[16] reported in 1925 fibrin studies in liver disease but did not include cases of obstructive jaundice. Weltmann and Neumayer[21] in 1925 reported from Germany the fibrin values in fifty-six patients with liver diseases. Twenty-seven of these showed increased values. They were chiefly cholelithiasis and neoplasm. Twelve others had normal values and the remaining seventeen had reduced determinations. The latter were chiefly diseases of the liver parenchyma. Baumann[20] in 1930 from Germany reported fibrin values well above normal in two cases of acute yellow atrophy, and two cases of carcinoma of the head of the pancreas with obstructive jaundice. The former bled to death post-operatively, one of the others bled post-operatively, and the fourth case developed hæmorrhages spontaneously. In addition to the above, several European investigators, including Wildegans,[22] Murakami, and Yamaguchi,[23] Isaac-Krieger, and Hiege,[24] and Schultz, and Scheffer[25] reported fibrin values in patients and animals with obstructive jaundice, but their results are of questionable value, because the method they used is not a quantitative one. It was described by Wohlgemuth[26] in 1910.

Method of Fibrin Determination.—There are several methods by which the blood fibrin may be determined. Schultz *et al.*[10] give a complete list of references. The most practical method is to change the fibrinogen to fibrin by causing the plasma to clot. This clot is readily handled and the amount of it may be determined either gravimetrically or by means of the Kjeldahl method. The determination of the fibrin by gravimetric means compares accurately with direct determination of the fibrinogen by precipitation with sodium sulfate,[17] and also with other methods.[5]

The method I have found the most satisfactory is the gravimetric method originally described by Foster, and Whipple[5] and later modified by Schultz *et al.*[10] I have added another slight modification. Instead of a 2 per cent. solution of sodium oxalate as an anti-coagulant employed in the collection of the blood, I have used a dry-powdered anti-coagulant. The advantage of this is that in computing the fibrin values and reading the hæmatocrit values one does not have to take into consideration any correction because of dilution of the sample of blood, due to the anti-coagulant.

The method I used in detail is as follows: Five to seven cubic centimetres of blood are withdrawn from a vein by syringe and needle. The blood is immediately put in a small bottle containing approximately 14 milligrams of powdered potassium oxalate. A thorough mixing by shaking the bottle prevents coagulation. The plasma is separated from the red corpuscles by centrifugalization. This is done in a graduated tube, so that the hæmatocrit reading is obtained. Two cubic centimetres of the clear plasma are then drawn off with a pipette, and mixed in a 50 cubic centimetre centrifuge tube with 40 cubic centimetres of a clotting solution containing 0.8 per cent. sodium chloride and 0.125 per cent. calcium chloride.

After a period of two to three hours at room temperature or twelve hours in the ice box, the fibrin of the plasma forms a coagulum. This is freed from the side of the tube with a glass rod. It is then collected either by means of a fine glass rod by which the fluid may be expressed from the fibrin, or as Schultz *et al.*[10] describe, by means of high-speed centrifugalization in which case the fibrin is compressed into a small white button. Some of the coagulums are so friable that the glass rod breaks them into many pieces. This makes the fibrin extremely difficult to collect by this means. In these

cases I found centrifugalization is the best mode of collection. The tough coagulums are more easily collected with a glass rod.

The next step is to press the fibrin between filter paper to express the excess water. The small pellet of fibrin is then transferred to a porcelain crucible and dried for one to two hours in an oven at 110° C. After cooling in a desiccator the crucible and fibrin are weighed carefully. The fibrin is then burned by placing the crucible over a Bunsen burner for five minutes. The crucible and ash are again cooled in a desiccator and then weighed. The difference in weight represents the amount of fibrin in 2 cubic centimetres of plasma. From this figure the amount of fibrin per 100 cubic centimetres of plasma and blood are readily computed by the following formulæ:

$$\frac{\text{Milligrams fibrin in 2 cubic centimetres of plasma} \times 100}{2} =$$

Milligrams of fibrin per 100 cubic centimetres of plasma

and

$$\frac{\text{Milligrams fibrin in 2 cubic centimetres of plasma} \times \text{percentage of plasma}}{2} =$$

Milligrams of fibrin per 100 cubic centimetres of blood.

Clinical Observations.—Blood fibrin studies were carried out on a series of fifteen patients with obstructive jaundice. (Table II.) Six had carcinoma of the pancreas occluding the common bile-duct, two carcinoma of the gall-bladder involving the common bile-duct, three hepatitis and an associated cirrhosis, one cirrhosis of the liver, one metastatic carcinoma of the liver involving the common bile-duct, one carcinoma of the ampulla of Vater, and one case of cholelithiasis with obstructive jaundice. The patients' ages varied from thirty to sixty-three years. The minimum duration of the jaundice was one week and the maximum was ten weeks. Eight cases had jaundice of six or more weeks' standing. The minimum degree of jaundice measured by the quantitative van den Bergh test was 12 milligrams of bilirubin per 100 cubic centimetres of serum and the maximum was 31 milligrams, indicating in all cases a high degree of obstructive jaundice.

Thirteen of the fifteen cases were operated upon. In five cases, exploratory laparotomy was the only operative procedure. Seven of the patients developed post-operative bleeding. In three of these, hæmorrhage played a major rôle in the cause of death, and in the other four it was of less importance, but a contributing factor.

TABLE II

Fibrin Values in Obstructive Jaundice

CASE I.—Diagnosis.—Carcinoma of gall-bladder with obstructive jaundice. Female, fifty-seven years old. Duration of jaundice.—7 weeks. Degree of jaundice.—18.75. Blood fibrin.—219–490. Plasma fibrin.—300–700. No. of determinations.—2. No hæmorrhage.

CASE II.—Diagnosis.—Carcinoma of gall-bladder with obstructive jaundice. Female, fifty-four years old. Duration of jaundice.—2 weeks. Degree of jaundice.—13.5. Blood fibrin.—527–1046. Plasma fibrin.—800–1275. No. of determinations.—4. No hæmorrhage.

CASE III.—Diagnosis.—Carcinoma of pancreas with obstructive jaundice. Female, forty-eight years old. Duration of jaundice.—6 weeks. Degree of jaundice.—30.0. Blood fibrin.—487–568. Plasma fibrin.—650–800. No. of determinations.—2. Hæmorrhage one plus.

CASE IV.—Diagnosis.—Carcinoma of pancreas with obstructive jaundice. Male, forty-nine years old. Duration of jaundice.—2 weeks. Degree of jaundice.—12.0. Blood fibrin.—357. Plasma fibrin.—700. No. of determinations.—1. No hæmorrhage.

CASE V.—Diagnosis.—Carcinoma of pancreas with obstructive jaundice. Male, thirty-eight years old. Duration of jaundice.—8 weeks. Degree of jaundice.—31.0. Blood fibrin.—487–536. Plasma fibrin.—650–800. No. of determinations.—3. Hæmorrhages four plus.

CASE VI.—Diagnosis.—Carcinoma of pancreas with obstructive jaundice. Male, forty-eight years old. Duration of jaundice.—6 months. Degree of jaundice.—15.0. Blood fibrin.—725. Plasma fibrin.—1150. No. of determinations.—1. No hæmorrhage.

CASE VII.—Diagnosis.—Carcinoma of pancreas with obstructive jaundice and cholelithiasis. Male, fifty-eight years old. Duration of jaundice.—10 weeks. Degree of jaundice.—12.0. Blood fibrin.—336. Plasma fibrin.—600. No. of determinations.—1. Hæmorrhage ten days later, just ante-mortem.

CASE VIII.—Diagnosis.—Carcinoma of pancreas with obstructive jaundice. Male, sixty-three years old. Duration of jaundice.—8 weeks. Degree of jaundice.—26.5. Blood fibrin.—420–612. Plasma fibrin.—600–800. No. of determinations.—4. Hæmorrhage four plus.

CASE IX.—Diagnosis.—Hepatites with obstructive jaundice and cholelithiasis. Female, fifty years old. Duration of jaundice.—1 week. Degree of jaundice.—12.0. Blood fibrin.—310. Plasma fibrin.—500. No. of determinations.—1. No hæmorrhage.

CASE X.—Hepatites with obstructive jaundice. Male, thirty years old. Duration of jaundice.—4 weeks. Degree of jaundice.—12.75. Blood fibrin.—341–558. Plasma fibrin.—550–900. No. of determinations.—5. Hæmorrhage three plus.

CASE XI.—Diagnosis.—Hepatites with obstructive jaundice. Male, fifty-one years old. Duration of jaundice.—7 weeks. Degree of jaundice.—24.75. Blood fibrin.—330–612. Plasma fibrin.—550–900. No. of determinations.—10. Hæmorrhage two plus.

CASE XII.—Diagnosis.—Cirrhosis of liver with obstructive jaundice. Male, fifty-five years old. Duration of jaundice.—2 weeks. Degree of jaundice.—12.4. Blood fibrin.—270–384. Plasma fibrin.—450–600. No. of determinations.—3. No hæmorrhage.

CASE XIII.—Diagnosis.—Metastatic carcinoma of liver with obstructive jaundice. Male, sixty-two years old. Duration of jaundice.—8 weeks. Degree of jaundice.—26.0. Blood fibrin.—620. Plasma fibrin.—850. No. of determinations.—1. No hæmorrhage.

CASE XIV.—Diagnosis.—Cholelithiasis with obstructive jaundice. Female, forty-eight years old. Duration of jaundice.—1 week. Degree of jaundice.—20.8. Blood fibrin.—570–600. Plasma fibrin.—1000. No. of determinations.—2. No hæmorrhage.

CASE XV.—Diagnosis.—Carcinoma of the ampulla of Vater. Female, fifty-two years old. Duration of jaundice.—8 weeks. Degree of jaundice.—9.0. Blood fibrin.—324. Plasma fibrin.—600. No. of determinations.—1. Hæmorrhage four plus.

Blood fibrins are given in milligrams per 100 cubic centimetres of blood, and plasma fibrins in milligrams per 100 cubic centimetres of plasma. Normal values are, blood fibrin, 166 milligrams; plasma fibrin, 321 milligrams.

Repeated fibrin determinations were made both pre-operatively and post-operatively, when possible. A total of forty-one samples of blood were examined for blood and plasma fibrin values. In the entire group no diminution of the fibrin values was found, instead there was a marked increase in most cases. The minimum blood and plasma fibrins were 219 and 300 milligrams respectively. The maximum values were 1,046 milligrams and 1,275

milligrams. The majority of the blood fibrins were in the neighborhood of 500 milligrams and the plasma fibrins lay between 600 and 800 milligrams. The mean values were 483 milligrams and 742 milligrams respectively. Compared with the mean normal values of 166 and 321 milligrams (*vide* Table I), the blood fibrin values in this group of cases with obstructive jaundice, are approximately three times as great, and the plasma fibrins are nearly two and one-half times the normal value.

Five of the cases which developed the typical hæmorrhagic diathesis of obstructive jaundice are of especial interest, as it was possible to study them

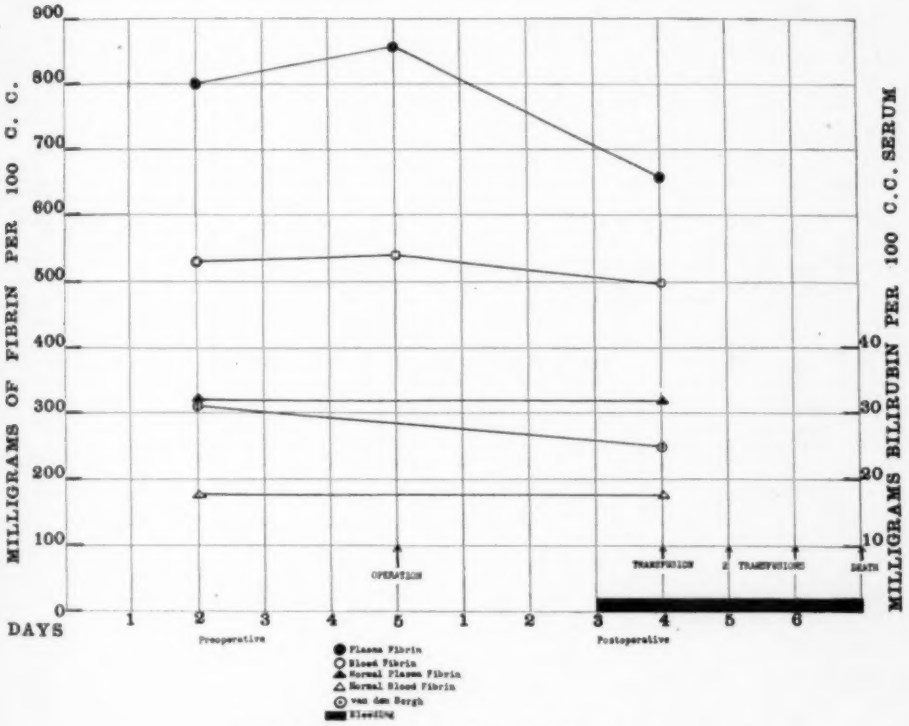

CHART I.—The blood and plasma levels in Case V.

before and during the bleeding stage. These were Cases III, V, VIII, X, and XI. (Table II.)

CASE REPORTS.—The following four cases with charts illustrate the high level of the blood fibrin which has been found in all these patients. I have chosen these four because they show the level before and during the actual bleeding.

(1) Case V, Chart I, shows the findings in a thirty-eight-year-old Irish workman, who entered the hospital complaining of jaundice of two months' duration without pain. He had a high degree of jaundice, 31 milligrams per 100 cubic centimetres of serum. The patient was placed on a high carbohydrate, low fat diet and was given three pre-operative injections of ten cubic centimetres of a 5 per cent. calcium chloride solution. At exploratory laparotomy under spinal anæsthesia a large distended gall-bladder was found with a small carcinoma of the pancreas occluding the common bile-duct. A cholecystogastrostomy was performed. Extreme care was taken to prevent hæmorrhage

at the suture line. A shoemaker's stitch was employed, using two needles and threads. This inner suture line was reinforced with a serosal stitch outside it. The abdomen was closed in layers without drainage. The patient stood the operation very well. Fluids were given post-operatively by clysis, vein and proctoclysis. Small amounts of water by mouth were started on the first day post-operative. On the third day post-operative he vomited 900 cubic centimetres of coffee-ground-like material. A nasal catheter was inserted and passed into the stomach. This was left in place as it continued to drain large amounts of bloody fluid. Within the next three days the patient received four whole blood transfusions, each one of 600 cubic centimetres. In spite of these, the bleeding continued, and death occurred on the seventh day following operation from uncontrollable hæmorrhage. Autopsy was not performed.

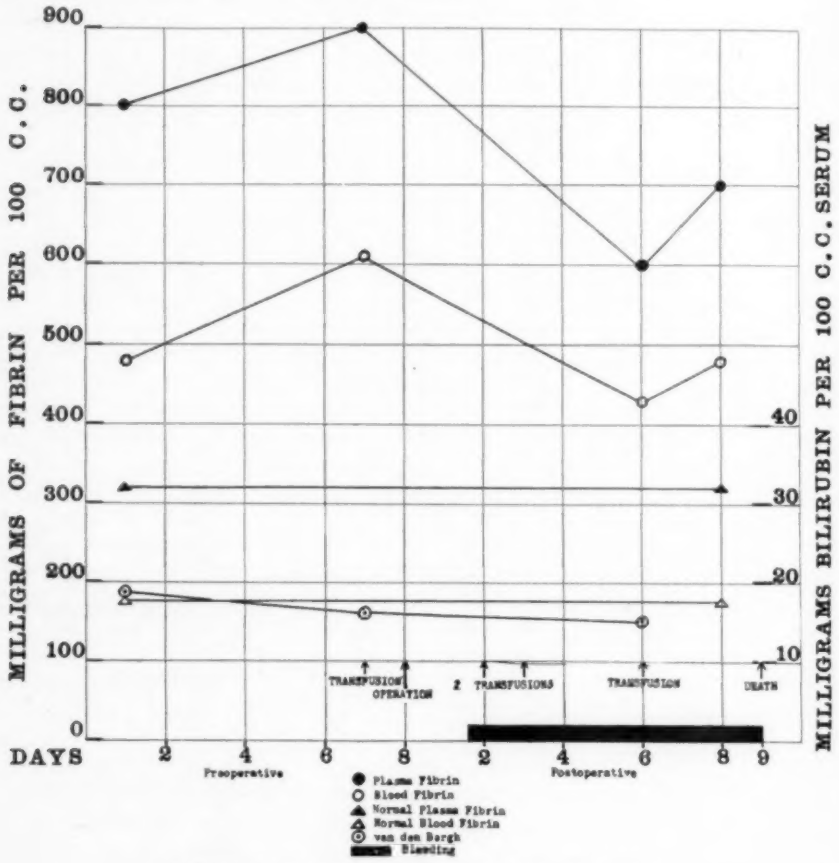

CHART II.—The blood and plasma levels in Case VIII.

Comment.—This patient died because of uncontrollable post-operative hæmorrhage and yet on three occasions, blood fibrin determinations showed no deficiency in the fibrin. The third estimation was done at the time bleeding was taking place, yet both the blood and plasma values are several times the normal values.

(2) Case VIII, Chart II shows the findings in a sixty-three-year-old man, who entered the hospital complaining of painless jaundice of eight weeks' duration, anorexia, nausea and general malaise. He had a high degree of jaundice with a serum bilirubin of 18.75 milligrams per 100 cubic centimetres of serum. A large distended gall-bladder and enlarged liver were palpable. After careful pre-operative preparation with fluids,

glucose and blood transfusion, operation was performed. Under spinal anæsthesia a moderate-sized carcinoma of the head of the pancreas was found, which was obstructing the common bile-duct. The gall-bladder was filled with white bile. A cholecystogastrostomy was performed using three layers of chromic O catgut. The abdomen was closed in layers without drainage. Small amounts of water were given beginning the first day post-operative. The fluid intake was maintained by a continuous intravenous drip of 5 per cent. glucose solution in normal saline.

On the second day post-operative the patient vomited a little dark red bloody fluid and stomach lavage yielded 1,000 cubic centimetres of the same material. A nasal

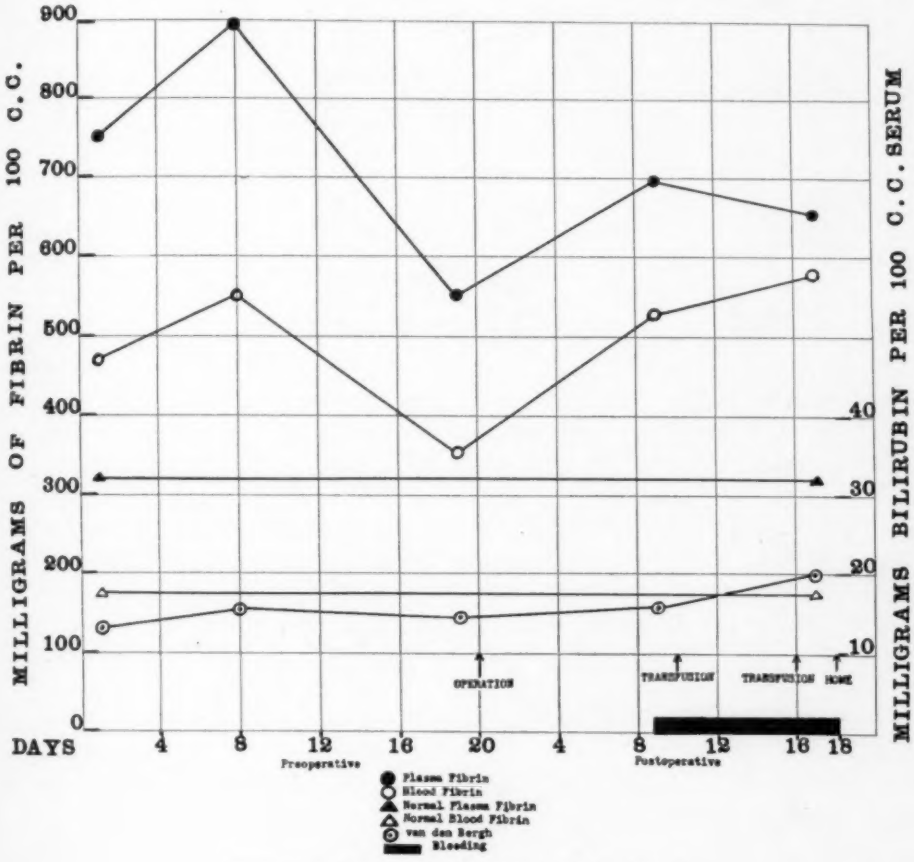

CHART III.—The blood and plasma levels in Case X.

catheter was passed into the stomach to drain off the fluid as it accumulated. Transfusions were given on the second, third, and sixth days post-operatively. The first two seemed to check the hæmorrhage temporarily, but the patient died on the ninth day post-operative from hæmorrhage and liver insufficiency. Bile was never demonstrated in the stomach contents. Autopsy confirmed the diagnosis, and in addition to the intrabiliary and gastro-intestinal hæmorrhage, there was considerable hæmorrhage around the cholecystogastrostomy with oozing into the peritoneal cavity.

Comment.—Blood and plasma fibrin determinations were done on four occasions, as the chart indicates. All of these are well above the normal value, even at the time hæmorrhage was taking place, thus showing that the hæmorrhage was not due to a lack of blood fibrin in this case.

(3) Case X, Chart III, shows the findings in a man of thirty years who entered the hospital because of painless, increasing jaundice of four weeks' duration. The serum bilirubin, according to the quantitative van den Bergh test, remained in the neighborhood of 13.0 milligrams. Stool examination on frequent occasions showed no bile. As a definite diagnosis could not be made, and because of persistent complete biliary obstruction, operation was advised. Exploratory laparotomy was performed under spinal anæsthesia three weeks after admission. No obstruction of the common bile-duct was found. A piece of liver was removed for biopsy which showed early biliary cirrhosis, thus accounting for the jaundice and clay-colored stools. Following

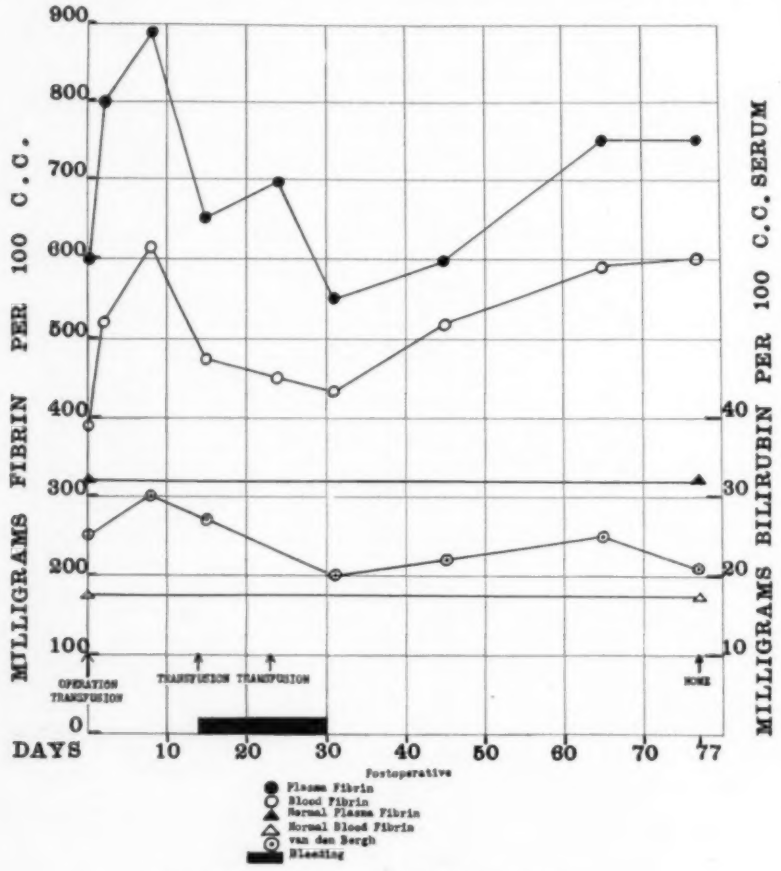

CHART IV.—The blood and plasma levels in Case XI.

the operation, the patient made a very slow recovery. The jaundice deepened considerably. On the ninth day post-operative, hæmorrhage from the wound was first noted. This became so alarming that two transfusions were given with partial control of the bleeding. The patient left the hospital the nineteenth day following operation, still bleeding from his wound. He died not long after leaving the hospital from hepatic insufficiency and cirrhosis of the liver.

Comment.—The obstruction of the biliary system in this case was not in the common bile-duct, but in the small biliary passages. The fibrin values, however, show much the same elevated level that the other cases of obstructive jaundice have shown. There was no diminution of them at the time of the post-operative bleeding.

(4) Case XI, Chart IV, shows the findings in a man of sixty-two years who

entered the hospital complaining of painless, increasing jaundice of seven weeks' duration. His stools were clay-colored and were bile negative. The jaundice was of severe intensity as the serum bilirubin was 25 milligrams according to the quantitative van den Bergh test. Exploratory laparotomy was done under ether anæsthesia. No obstruction of the common bile-duct was found. The liver was large and showed a moderate degree of cirrhosis. The patient's convalescence was uneventful until about the fourteenth day, when bleeding was noted from his wound. This was controlled by two transfusions of whole blood, but not until it had lasted about two weeks. The patient was kept in the hospital in all about eleven weeks. His jaundice persisted. Continuous intravenous administrations of 5 per cent. glucose in normal saline was used, which I feel prolonged his life. He had no more actual bleeding, although he developed a number of areas of ecchymosis on his right arm. These were noted about fifty-three days following operation, and remained about a week. These, along with a very rapid sedimentation rate, still indicated a definite hæmorrhagic diathesis. He was eventually discharged from the hospital and died about six months later from cirrhosis of the liver with complete biliary obstruction.

Comment.—This case is similar to the preceding one. On all occasions the fibrin was found to be greatly elevated. The highest point was reached immediately post-operatively, but it was still markedly elevated during the bleeding stage and also when he developed the ecchymotic areas on his arm. At no time in his long stay in the hospital was there any evidence of a fibrin deficiency.

Discussion.—The hæmorrhagic diathesis of obstructive jaundice has not as yet been satisfactorily explained. In studying the possible causes of this serious complication, it seemed possible that a lack of fibrin in the blood might be an important factor, since in severe liver destruction there exists a marked diminution of the blood fibrin and an associated hæmorrhagic diathesis. Accordingly, blood fibrin studies were carried out on a series of fifteen patients with obstructive jaundice. These cases were selected because they all had a high degree of obstructive jaundice. Seven of this group, or 46.7 per cent., developed post-operative hæmorrhage. In three of these, or 20 per cent. of the entire group, hæmorrhage played a major rôle in the cause of death.

Repeated fibrin determinations were made according to the modification of the Foster and Whipple method described by Schultz, *et al.*[10] Forty-one determinations were made in this series of cases. The blood fibrins varied from 219 to 1,046 milligrams per 100 cubic centimetres of blood and the plasma fibrins from 300 to 1,275 milligrams per 100 cubic centimetres of plasma. The mean blood and plasma fibrin values were respectively 483 milligrams per 100 cubic centimetres of blood and 742 milligrams per 100 cubic centimetres of plasma. In Case II on one occasion the blood fibrin was 1,046 milligrams. This high value was probably due to the fact that the patient had a diffuse broncho-pneumonia at the time the estimation was made. No case showed a fibrin value below normal. Compared to the mean normal fibrin values the mean blood and plasma fibrin values in this group of cases are respectively three, and two and one-half times as great.

Fibrin determinations were made pre-operatively and post-operatively. Immediately following operation there was a transient rise in the fibrin level in a few of the cases. This temporary rise was probably due to operative

wounds and low-grade pulmonary infections, as both these conditions have been shown experimentally in dogs to increase the fibrin level.[10] In the majority of cases the fibrin level remained elevated. There was no noticeable diminution of it, even up to the time of the patient's death.

Of especial interest were the seven cases which developed post-operative bleeding. In five of these, determinations were made before and during the actual bleeding. Comparison of the fibrin levels before and during the bleeding, (see Table III) show that there was a slight decrease of the latter in four of these cases. In the fifth case the average fibrin value was higher during the bleeding. After the hæmorrhage stopped in this case the fibrin level dropped even lower than before its occurrence. These variations before, during, and after hæmorrhage are probably of little significance. The important fact, however, is that during the bleeding stage there was no marked decrease in the fibrin level, and that in all cases the amount of fibrin was two to three times the normal value.

TABLE III

Fibrin Values in Cases with Bleeding

Case	Before Hæmorrhage		During Hæmorrhage		After Hæmorrhage	
	Blood Fibrin	Plasma Fibrin	Blood Fibrin	Plasma Fibrin	Blood Fibrin	Plasma Fibrin
3	568	800	487	650	—	—
5	531	825	487	650	—	—
8	546	850	450	650	—	—
10	457	733	447	675	—	—
11	384	600	461	675	375	575

Blood fibrins are given in milligrams per 100 cubic centimetres of blood, and plasma fibrins in milligrams per 100 cubic centimetres of plasma. Normal values are, blood fibrin, 166 milligrams; plasma fibrin, 321 milligrams.

CONCLUSIONS

(1) Fifteen patients with obstructive jaundice were found to have blood and plasma fibrin levels several times the normal value.

(2) In six patients who developed post-operative bleeding the fibrin levels were several times the normal values even at the time of actual bleeding.

(3) In obstructive jaundice, there is apparently no deficiency in the blood fibrin.

(4) The hæmorrhagic diathesis of obstructive jaundice is not explainable by a quantitative deficiency of the blood or plasma fibrin.

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THE SURGICAL TREATMENT OF ACUTE CHOLECYSTITIS

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The importance of early operation in acute appendicitis has been so definitely established, and has been commented upon so frequently, that it has been generally accepted by members of the medical profession. In the case of acute inflammation of the gall-bladder, there seems to be no such unanimity of opinion. Very frequently, unless the attack is fulminant, the physician counsels delay in this condition, hoping that by time-honored conservative treatment, operation may be postponed until an interval, or avoided indefinitely. While it is well known that such a policy is frequently attended by success, we are convinced that it has been insufficiently emphasized that in many instances the inflammatory process either fails to subside, or becomes more intense, leading to serious pathological lesions, complications, increased distress to the patient, prolonged convalescence, and even death. Let us make it clear that we are not considering cases of acute gall-bladder colic such as occur in the course of a chronic cholelithiasis, but only acute inflammatory lesions of the gall-bladder. The usual symptoms and signs of such a condition are pain in the abdomen, nausea, vomiting, fever, leucocytosis, and tenderness over the gall-bladder, usually associated with muscle spasm or rigidity. A distended gall-bladder may often be palpated provided the muscle response is not too intense. A slight but definite jaundice is not infrequent, due usually to associated cholangiitis. Pathologically, there is found a distended gall-bladder, surrounded by fibrinous adhesions, the wall red and œdematous. The cystic duct is usually occluded by adhesions, by inflammatory œdema, or by an impacted stone. As the disease progresses, the viscus may become filled with a hæmorrhagic or purulent exudate, and subsequently there may develop gangrene or perforation of the wall.

Given a patient with such a condition, what treatment should be instituted—watchful waiting or early surgical interference? To answer this question satisfactorily, there are several things we should know. First, what is the likelihood that the attack will subside; second, what are the chances that the attack will fail to subside or will become worse; third, what will be the ultimate outcome if the attack does subside spontaneously; and fourth, are there any advantages of early as compared with late operation? As regards the first question, it is generally agreed that many of the milder cases subside quickly and spontaneously, but as far as I am aware there are no available figures on which to estimate the percentage that may be expected to do so. Likewise in regard to the third question—namely, the incidence of subsequent trouble—there are no reported figures. I am convinced, however, that a large proportion of those who have had an acute inflammatory

lesion of the gall-bladder which subsided, will have subsequent and recurrent disability finally leading to operation. As regards the second and fourth questions, there is some small but suggestive statistical evidence. In an attempt to answer these questions we have recently reviewed the records of eighty-nine patients admitted to the Cincinnati General Hospital during the years 1925–1930, inclusive, in whom a diagnosis of acute cholecystic disease was made and who subsequently were operated upon. In this group there were seventy females and nineteen males. The age incidence is shown in Table I.

TABLE I

	Age					
	Less Than 20	*20–29*	*30–39*	*40–49*	*50–59*	*60+*
No. of patients	2	14	17	29	14	11

The average temperature was 100.2° F.; average pulse, 98; average leucocyte count, 15,766. The highest temperature was 103.4° F.; highest pulse, 120; highest leucocyte count, 31,000. The lowest temperature was 97° F.; lowest pulse, 60; and lowest leucocyte count, 6,500. There was found a close correlation between the leucocyte count and the severity of the clinical and pathological condition. In all the cases with empyæma of the gall-bladder, the leucocyte count was more than 15,000. The duration of symptoms before admission was less than twenty-four hours in twenty-one cases, one day to one week in twenty-four cases, and more than one week in forty-four cases.

Thirty-five of these patients were operated upon immediately after admission. In this group, the shortest duration was three hours, the longest ten days, the average three days. When these cases were analyzed according to the duration of the attack, the following observations were made:

TABLE II

35 Cases Operated upon Immediately after Admission

		Duration of Attack		
		Less Than 48 Hours	*2–5 Days*	*More Than 5 Days*
Number of cases		12	15	8
Average number of days in hospital		22.1	24.1	24.7
Deaths		0	1	2
Mortality, per cent		0	6.6%	25%
Pathological findings	Simple acute cholecystitis	11	5	0
	Uncomplicated empyæma	0	9	1
	Empyæma with abscess	0	0	2
	Empyæma with gangrene	1	1	4
	Empyæma with rupture	0	0	1

These patients were all definitely ill at the time of admission, so ill that there seemed to be no justification for delaying operation. The gall-bladder was removed in twenty-eight cases, drained in seven cases. Of the three that died, one had a cholecystectomy and two a drainage operation. In all

those that died there was empyæma complicated by gangrene of the wall of the bladder or the formation of abscess outside of it. One death occurred thirteen hours after operation from coronary sclerosis, one on the fifth day from bronchopneumonia, and one on the fourteenth day with an intra-abdominal abscess and a pancreatic abscess obstructing the common duct. The total mortality was 3 in 35, or 8.5 per cent.

The remaining fifty-four patients were observed for a period of twenty-four hours to twelve days after admission and before operation. This delay was made either because the patient refused operation or because it was the opinion of the attending or resident staff that the attack was comparatively mild and might subside. In this group of fifty-four patients, analysis shows that twenty, or 37.7 per cent., improved, the attack subsided, and they were subsequently operated upon in an interval; nineteen, or 35.1 per cent., failed to change significantly and at the time of operation were in essentially the same status as at the time of admission; fifteen, or 27.7 per cent., became definitely worse while under observation and suitable expectant treatment. In this last group four had a perforation of the gall-bladder at the time of operation and certainly in three instances the perforation occurred while the patients were on the wards. It is seen that of the fifty-four patients, in thirty-four, or 62.9 per cent., the attack either failed to subside or became worse.

An attempt was made to discover the reason why the attack failed to subside in these thirty-four instances. This could not be determined very satisfactorily, the only available data being the findings at operation, plus the investigation of the pathological specimen in the laboratory. It was found that in the cases that did not subside, there was generally a serious infection of the gall-bladder associated usually with an obstruction of the cystic duct. In the instances in which the attack subsided, less marked pathological change existed at the time of operation than in those in which there was failure to subside. No definite finding was made, however, which would enable us to predict in the future which cases would be likely to subside, and which become worse. Tabulation of the pathological findings at operation is presented in Table III.

TABLE III

Operative Findings in 54 Cases Treated Expectantly for One to Twelve Days Before Operation

Clinical Course During Observation	*Total Cases*	*Chronic Cholecystitis*	*Acute Cholecystitis*	*Uncomplicated Empyæma*	*Abscess Outside Gall-bladder No Perforation Demonstrated*	*Empyæma with Gangrene*	*Empyæma with Rupture*
Improvement...	20	13	4	1	1	0	1
No change.....	19	0	13	5	1	0	0
Worse.....	15	0	3	6	0	2	4

It can be seen that of the twenty cases that showed clinical improvement, thirteen showed only chronic lesions at operation, *i.e.*, the attack had un-

questionably subsided. Of the nineteen who showed no significant change in their clinical condition, thirteen showed simple acute inflammation, and six showed more serious lesions—empyæma and abscess formation. Of the fifteen who clinically became worse, only three showed uncomplicated acute changes, the rest serious pathological lesions—empyæma, gangrene and rupture. As was previously mentioned, this does not demonstrate the cause of failure of an attack to subside, but does show that it is the serious inflammatory lesions which are most prone to persist. Since empyæma of the gall-bladder was found almost exclusively in cases that failed to show clinical improvement, it is presumptive evidence that once this condition has developed it will persist in the majority of cases until relief is obtained by operative interference. In this connection it is apropos to reëmphasize the important correlation between the leucocyte count and the serious inflammatory lesions of the gall-bladder. In this series, the leucocyte count was above 15,000 in every case of empyæma of the gall-bladder.

Since in only two of these patients was the duration of the disease less than two days, they have been divided according to whether the attack had lasted less than one week or more than one week. Using this criterion, the following findings were made:

TABLE IV

		Total Duration of Attack Before Operation	
		Less Than One Week	*More Than One Week*
Number of cases		18	36
Average days in hospital—post-operative		25.2	27.2
Deaths		1	3
Mortality, per cent		5.5%	8.33%
Pathological findings	Chronic cholecystitis	4	11 (2 with abscess)
	Acute cholecystitis	10	10
	Uncomplicated empyæma	4	8
	Gangrene	0	2
	Rupture	0	5

The total mortality in the eighty-nine cases was seven cases, or 7.8 per cent. Three of the deaths occurred among the forty-five cases whose attack had lasted less than one week (mortality 6.66 per cent.), and four of them in the forty-four cases in which the attack lasted more than one week (mortality 9 per cent). In considering mortality in relation to duration of the attack, it is interesting to note that Miller,[3] in 1930, found that in 200 cases of acute gall-bladder treated at the Massachusetts General Hospital, the average duration of the attack in twenty-seven fatal cases was fifteen days, while in 173 who recovered the average duration was 8.3 days. Table V shows the relationship between the mortality and the pathological lesion in our series of eighty-nine cases, all of whom had an admission diagnosis of acute cholecystitis.

TABLE V

Mortality in 89 Cases in Relation to Pathological Lesion

	Total Cases	*Deaths*	*Mortality, %*
Chronic cholecystitis	15	1	6.6
Simple acute cholecystitis	36	2	5.5
Uncomplicated empyæma	22	1	4.5
Empyæma with gangrene or rupture	16	3	18.7

This shows the sharp rise in the mortality in association with gangrene and rupture of the gall-bladder, and is in agreement with the published findings of others. For example, Alexander[1] reported twenty cases of rupture of the gall-bladder with a mortality of 50 per cent. in those with acute free perforation, and a mortality of 25 per cent. with subacute or walled-off perforation.

The data presented have shown that delay in operating in certain cases of acute cholecystitis influences unfavorably the development of serious complications, and as these develop the mortality rises. It is possible to present evidence of additional advantages of early operation. For this purpose we present here in Table VI the findings of H. F. Graham[2] of 198 cases of acute cholecystitis from the Methodist Hospital of Brooklyn, N. Y.

TABLE VI

198 Cases of Acute Cholecystitis Reported by Graham

	Duration of Attack Before Operation	
	Less Than 48 Hours	*More Than 48 Hours*
Total number of cases	20	178
Mortality	5%	6.2%
Average days in hospital	19.5	26.4
Average number of dressings	4⅓	10½
Incidence of post-operative complications	5%	18%

These statistical reports of fairly large groups of patients answer, we believe, questions two and four postulated earlier in this paper. They show that in a majority of patients admitted to a general city hospital with acute inflammatory lesions of the gall-bladder the attack failed to subside under suitable conservative treatment. It has also been shown that early operation reduces the hospital stay, shortens the convalescence, probably reduces the number of dressings, the incidence of complications and the mortality. These, we believe, are the advantages to be expected of early operation.

One important point about which no statistical data can be collected is the technical difference between cholecystectomy done in the acute stage and in the interval. Each of the ten surgeons who operated on the eighty-nine patients in our report is of the opinion that the operation of cholecystectomy is more easily performed, as a rule, in the acute stage than in an interval. During the acute stage it is often surprising how easily the adhesions surrounding the gall-bladder and ducts can be separated, and the gall-bladder freed from the liver. On the other hand, after the attack has subsided, the adhesions formed during the attack become more and more fibrous and ad-

herent. During the acute stage, old adhesions seem to become less firmly attached, possibly due to increased vascularity and œdema. At any rate, it is rare to find an acutely inflamed gall-bladder which is as difficult to free as the average chronically inflamed one. The incidence of post-operative wound infection is probably somewhat greater in patients operated upon during the acute stage, but in our experience such infection has not been severe nor led to serious consequences, and it is our opinion that this aspect can be disregarded. We have also found that it is usually possible to remove the gall-bladder except in the very late cases with extremely ill patients, or those with massive adhesions, localized abscess, *etc.* In our series, the gall-bladder was removed in seventy-seven cases with five deaths, a mortality of 6.5 per cent.; drainage was done in twelve instances with two deaths, a mortality of 16.6 per cent. The higher mortality in the cases with drainage was undoubtedly due to the more serious condition of the patients.

The above presentation has made it clear that we advocate early operation in acute cholecystitis. We do not believe, however, that immediate operation should be recommended as a routine in all cases as soon as the diagnosis is made. We try to judge each case on its individual merits, realizing that the longer an attack persists the more dangerous is the condition likely to become. If the attack is fulminant from the start, if it fails to subside promptly, or if it increases in intensity while under observation, early operation is indicated and offers definite advantages.

SUMMARY

Eighty-nine cases of acute-gall-bladder disease are reviewed. These have been divided into two groups, one of thirty-five cases operated upon immediately after admission, and another of fifty-four cases observed from one to twelve days before operation. In the group held under observation, only twenty, or 37.7 per cent., showed improvement, and in these subacute or chronic inflammation was found at operation. Nineteen, or 35.1 per cent., showed no significant change in signs or symptoms during the period of observation, and in them uncomplicated acute cholecystitis and empyæma were the lesions most frequently found at operation. Fifteen, or 27.7 per cent., became definitely worse while under observation, and in them empyæma, gangrene and rupture of the gall-bladder were found. The total number of cases in the second group which failed to subside was, therefore, thirty-four, or 62.9 per cent. The average leucocyte count was 15,766 for the entire series. In all cases of empyæma it was above 15,000. The incidence of serious pathological lesions and the mortality were found to rise with the duration of the attack. With early operation the hospital stay and the mortality were less than with late operation.

CONCLUSIONS

In acute inflammatory gall-bladder disease, a high percentage of cases fails to improve under conservative, *i.e.*, non-operative treatment.

Empyæma of the gall-bladder is usually associated with a high leucocyte count (15,000 or higher), while the fever may be very variable.

When empyæma of the gall-bladder once develops it is unlikely to subside spontaneously and may progress to gangrene and rupture of the wall. When these complications occur, the mortality rate rises rapidly.

It is, therefore, recommended that in acute infections of the gall-bladder immediate operation be performed if the symptoms are severe and particularly if there is associated high leucocytosis. Early operation is also indicated if the attack fails to subside promptly.

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INTRAMURAL CALCIFICATION OF THE GALL-BLADDER

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A multiple number of causes have been assigned for intramural calcification of the gall-bladder. The most important of those listed are the following:

(*a*) Ulcerative cholecystitis with inflammatory exudate production causing obstruction of the lymphatics and of bile passing through the cystic duct.

(*b*) A second view is given that the calcareous processes result from phlegmonous exudate forming abscesses in the wall (Aschoff, Kerr, Flörchen[1]).

(*c*) Intramural formation of stones in his ducts may result in an extension of the process to the wall (Aschoff[1]).

(*d*) Extravasation of blood-cells and hæmorrhage in the gall-bladder wall may mobilize calcium salts irregularly within the wall (Davis[2]).

(*e*) Calcification may be due to cholelithic catarrh and inflammatory products of long duration (Mayo Robson,[3] Rolleston,[4] Delafield and Prudden[5]).

(*f*) Extreme resorption of bone may result in widespread deposits of calcareous salts, particularly in the gall-bladder (Adami[6]).

(*g*) Calcification generally occurs in vascular disorders of tissues. Local necrosis or fibrosis antedates intercellular calcification (Stengel and Fox,[7] MacCallum[8]).

(*h*) Calcium is deposited in the gall-bladder as a result of long-continued irritation (Moynihan[9]).

The infrequency of occurrence of intramural calcification of the gall-bladder wall is confirmed by literature and communications recently received from authors who have reported studies of a series of gall-bladders by X-ray and surgical means. In nine well-known text-books of surgery or pathology the process is not mentioned. In 8,695 cases of gall-bladder pathology reported by nine writers, calcification of the wall is not recorded.

Flörchen[1] quotes two cases reported by Bitzengiger in a series of 1,200 gall-bladder operations. In both of these cases the history was described as typically characteristic of cholangitis, being of short duration with elevation of temperature.

In one case a large gall-bladder ten centimetres by four centimetres with stony or button firmness like porcelain was found. The serosa was white and definitely separated from the other layers. No mucous membrane was present. The calcareous deposits were in the muscular and submucosal coats, particularly marked in the layers of the muscularis. In the cavity there was a cholesterin stone. A secondary finding of cancer of the stomach was noted. The clinical symptoms in the two cases were so unimportant as to hardly indicate operative procedures.

Baless and Skinner[10] have reported one case, a woman fifty-two years of age, who had not been ill for twenty-seven years. Her symptoms, lasting for two days, were at first suggestive of appendicitis, later changing to those of gall-bladder disease. The X-ray showed calcification of the bladder wall and a calculus formation. The lumen was filled with thick bile.

Holden[11] has reported one case, a woman of fifty-two years of age, who had a history of severe pain thirty years prior to gastric distress and gas formation. The X-ray showed a circular shadow under the surface of the liver. At operation the gall-bladder was found to be brittle and generally calcified and there was a stone within the lumen. There was also chronic ulcerative cholecystitis present.

Moore[12] reported two examples of intramural calcification in old patients who were not submitted to operation (hence the cases were not unequivocally established). The X-rays of these patients were published in Diseases of the Gall Bladder and Bile Ducts, by Graham, Cole, Copher and Moore; Lea and Febiger, Philadelphia, 1928.

Kirklin[13] reports under date of November 3, 1931, that during the past seven years at The Mayo Clinic they were able to find only four cases of intramural calcification of the gall-bladder that had been rayed and proved at operation to have had definite intramural calcification. The total number of gall-bladder operations during this period was 5,826.

Case I.—Woman; aged fifty-eight years. Providence Hospital, No. 1749-N. Chief complaints, indigestion, nausea, sour stomach, vomiting, and pain in right upper quadrant. A history that during childhood she had measles, and at sixteen years had inflammatory rheumatism which confined her to bed for three months. The present illness began about five years ago with stomach sickness unaccompanied by pain; this sickness continued at intervals for three years; there was no distress after taking food, but water seemed to aggravate the stomach sickness.

During the last two years pain developed, occurring in attacks; there was radiation of this pain over the entire shoulder and frequently to the back and left side, passing upward between the scapulæ. Nausea and vomiting occurred often and at most any hour, and were followed by sour taste in the mouth and emesis of a yellowish material. During the past few years there had been much belching of gas and a loss of several pounds in weight. About a year ago there was an attack of pain and distress lasting three weeks. Vomiting and resting in the prone position gave relief from this pain, but standing aggravated the pain.

Father died at seventy-four years from Bright's disease.

Mother died at sixty-nine years from carcinoma of stomach.

One brother and four sisters are living and well.

Menstrual History.—Negative. Menopause occurred six years ago.

Examination was essentially negative, except for the following: Nasal septum was deviated to the right. All teeth had been removed from the mouth. Tonsils were atrophied. Mucous membranes of the mouth showed some pallor. Tongue was slightly coated and showed some tremor when protruded. Heart was enlarged several centimetres to the left and gave a blowing systolic murmur at the apex; but could be heard in the other three areas. Blood-pressure was 120/75.

Abdomen was slightly enlarged and there was a questionable tumor in the upper abdomen in the mid-line. The liver border was palpable two to three centimetres below the right costal margin. There was some tenderness over the pyloric area of the stomach.

Laboratory Examination.—Urine: specific gravity, 1.010, trace of albumin, trace of sugar.

Blood: hemoglobin, 70 per cent.; red blood-cells, 3,800,000; white blood-cells, 5,300.

At operation the gall-bladder was found surrounded by numerous adhesions; the fundal portion ruptured during removal and considerable milky fluid escaped into the abdominal cavity.

The removed gall-bladder (Fig. 1) contained in its neck an oval-shaped stone, which measured four centimetres in length and three centimetres in cross diameter; the stone

was slightly encrusted and adhered slightly to the bladder wall. The bladder wall was stiffened and had a fragile character with deposition of inorganic material in all layers of the wall. Palpation gave the sensation of eggshell resistance and at one place there was fracturing of the wall. The wall had a thickness of seven millimetres, and where it surrounded the stone, three millimetres.

Microscopical Examination.—The mucosal portion of the wall had been completely destroyed; the muscularis was intact only in certain areas; in these areas the muscle bundles showed atrophy with the cell nuclei almost completely obliterated; the fibrous layer was narrower than normal and its cells exhibited advanced atrophy with extensive loss of cell nuclei; the blood-vessels were sclerotic, the intimal layer being particularly thickened, so as to almost close the lumina; the muscle cell nuclei were better preserved than were those in the muscularis or fibrous layers.

Distributed extensively through other portions of the wall there were areas of

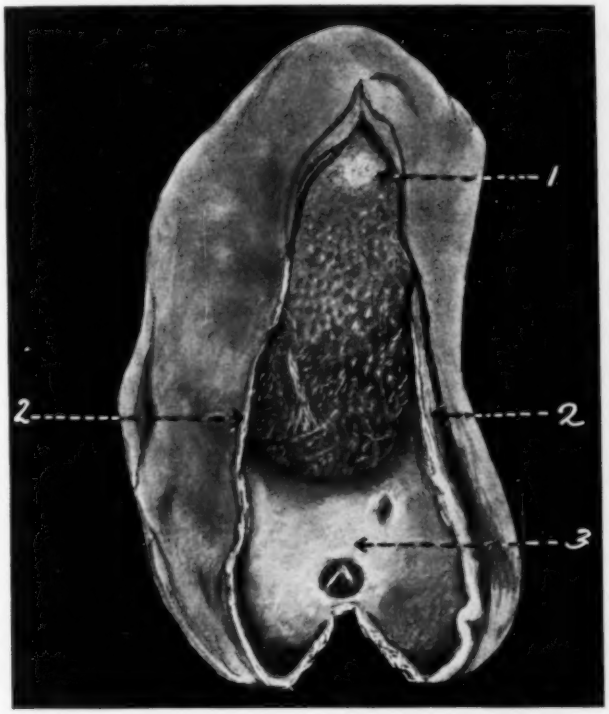

FIG. 1.—Intramural Calcification of the Gall-Bladder. 1—Calculus. 2—Intramural calcification. 3—Calcification evident in mucosa.

fibrosis, local aggregations of lymphocytes, depositions of calcium salts and of fascicular fatty crystals; the local areas of infection occurred in all three layers, the fibrosis with hyalinization, calcification and fatty degeneration were most marked in the zones of the muscularis and mucosa; there was a very constant relation between the fibrosis, hyalinization, infection, calcification and fatty degeneration.

(Osmic Acid Fat Stain.) Exhibited both localized areas of fat masses and also zones containing small globules of fat, and also some fat in distinct fascicular crystalline forms; in certain areas the tissue was in an early stage of degeneration and the particles of fat were very small and stained faintly.

Diagnosis.—(1) Intramural calcification of gall-bladder wall with associated cholesteatomatous degeneration and fibrosis, hyalinization and receding chronic cholecystitis. (2) Cholelithiasis (single cholesterin stone formation).

CASE II.—(By courtesy of Dr. A. L. Amolsch.) A white, obese, well-nourished, well-developed woman, aged forty-four years, mother of two children.

History.—The record showed no epigastric pain or gas but only habitual constipation. The terminal symptoms were acute epigastric and lower abdominal pain which subsided for a time, then recurred and localized in the lower abdomen and was accompanied with diarrhœa. The patient died with symptoms of intestinal obstruction and pelvic peritonitis. At autopsy the intestines were found angulated and adherent. In different areas abscesses were walled off and a general plastic exudative peritonitis prevailed. The origin of this was tubo-ovarian.

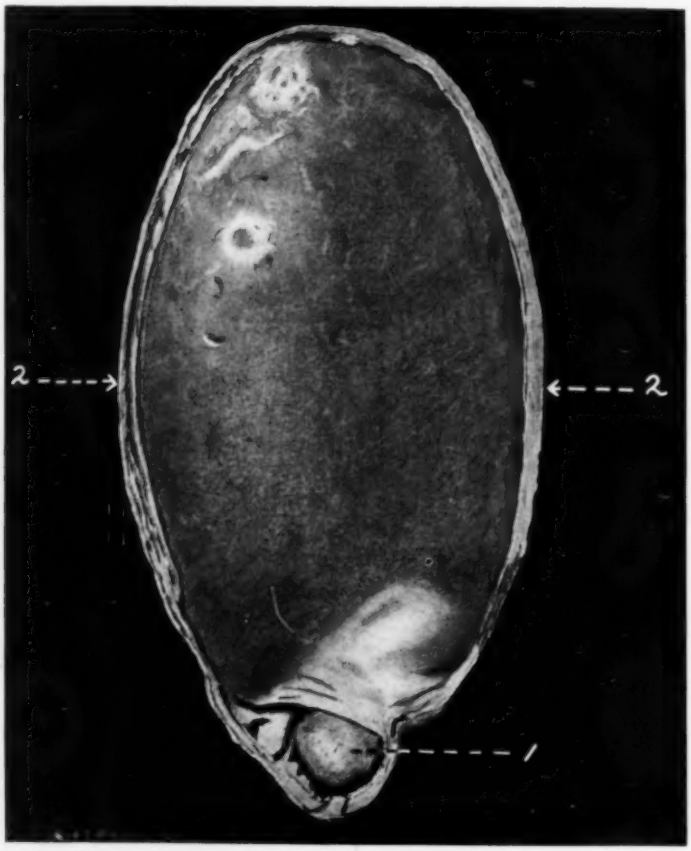

FIG. 2.—Intramural Calcification of Gall-Bladder. 1—Calculus. 2—Intramural calcification.

The gall-bladder (Fig. 2) was enlarged (7.5 by 4.5 centimetres by 2 millimetres in thickness) and of whitish color. Its wall was tense, fibrosed and calcified. The cystic duct was sharply angulated and it contained an impacted cholesterin stone which produced obstruction and inflammatory changes.

The mucosal surface was pale and the folds were obliterated. In the cut edge of the bladder wall laminations of inorganic depositions were plainly shown as eggshell-like formations. By translucent light and viewed from the mucosal surface mottled hard whitish areas were seen scattered throughout the entire wall. By palpation the wall imparted an eggshell and fibrous charactered impression.

Microscopically, the tissue had lost almost all of the mucosa and muscularis was pale, fibrosed and almost unrecognizable. The fibrous layer when stained with osmic acid displayed globules of fat in place of the normal structure. The entire tissue was

extensively hyalinized and in numerous areas there were aggregations of infiltrated lymphocytes. Calcification was irregularly present in the middle and outer tissue zones.

Diagnosis.—(1) Chronic cholecystitis. (2) Cholangitis with stone formation in the cystic duct. (3) Intramural calcification and lipoidal degeneration of the gall-bladder wall.

Conclusions.—(1) The microscopical studies of two cases of intramural calcification of the gall-bladder showed positive evidence of long-standing cholecystitis and depositions of readily staining fat in considerable quantities. A very constant relation of fibrosis, hyalinization, infection, fatty degeneration and calcification obtained in each case.

(2) The physical character of each bladder wall when deeply palpated gave a broken eggshell sensation to the palpating fingers.

(3) Specifically diagnostic subjective clinical symptoms of intramural calcification are unknown. A small percentage of cases with cholecystitis of long duration and single stone formation may have calcification involving the bladder wall. X-ray delineation of a calcifying intramural process is the most satisfactory diagnostic means available.

(4) The gall-bladder wall may be easily broken by manipulation during its removal and a milky fluid contained in the bladder lumen freely spilled. This fluid is rich in fat and is usually sterile and causes no harm from leakage into the peritoneal cavity.

(5) In cases of long duration malignancy should be considered as a sequel to the irritation given by the degenerated tissues, particularly in the parts contiguous to the calcified masses.

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ACUTE PANCREATIC NECROSIS AND ITS SEQUELÆ

A CRITICAL STUDY OF THIRTY CASES

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The development of pancreatic surgery since Körte's treatise,[1] in 1898, through the monographs of Heiberg,[2] in 1914, Gross and Guleke,[3] in 1924, Schmieden and Sebening,[4] in 1928, up to its present status, described in Wolfer's[5] and Heller's[6] reviews, contains all the clinical bibliography on the subject. In spite of the vast amount of experimental work and case reports the uncertainty of diagnosis and the high mortality have remained practically unchanged. Table I includes only three large statistics, and shows that, in comparison with other fields in surgery, very little progress has been made in reducing the mortality of acute necrosis of the pancreas.

Table I

Mortality of Acute Pancreatic Necrosis

Author	Year	Number of Cases	Mortality Per Cent.
Körte	1911	103	60
Guleke	1924	437	52.2
Schmieden and Sebening	1927	1278	51.2

In the present study, thirty cases of acute pancreatic necrosis or their sequelæ were analyzed, that entered the Evanston and Wesley Memorial Hospitals between 1920 and 1930. It represents the material of nine surgeons and is thus a fair average of what a patient may expect when struck with acute necrosis of the pancreas and taken to a large general hospital. Obviously the pre-operative management, the diagnosis, the operation and after treatment were not uniform in this series; however, while on a small material, this offered an excellent basis of comparing various methods of management. As a close correlation of physiological and pathological data with clinical observations is singularly lacking in most of the publications, we tried to point these out, with the hope that they may aid in lowering the mortality and untoward sequelæ of this disease.

Age and Sex of Patients.—(Table II.) Half of the patients (fifteen) were between the ages of forty and sixty. Schmieden and Sebening mention the case of a thirteen-year-old girl with a common-duct stone, who developed an acute necrosis. Cases are on record at the ages of two and one-half, three, four and seven years.[7] However, the occurrence of the disease below twenty years must be very rare and was not observed in our series.

TABLE II

Age and Sex of Patients

Decades	Number of Cases
20–30	6
30–40	5
40–50	7
50–60	8
60–70	3
80–90	1
	30

Half of the patients were between the ages of 40–60.

Number of men	12
Number of women	18

The incidence of sex was twelve male to eighteen female patients. The slight preponderance of the female sex is present in all of the large statistics and is undoubtedly due to the important rôle of gall-bladder disease in the etiology.

The Clinical Picture.—Recurrent attacks of upper abdominal or right hypochondriac pains were elicited in nineteen patients, whereas eleven denied having any previous attacks. The clinical symptoms of the last attack for which the patient came to the hospital were as follows. (Table III.)

TABLE III

Clinical Signs and Symptoms of Acute Pancreatic Necrosis

Symptoms and Signs	Number of Cases
Pain in epigastrium with general irradiation	30
Reverse peristalsis (nausea, vomiting, acute gastric dilatation)	23
Jaundice or clay-colored stools	12
Pain in right upper quadrant and right shoulder	10
Pain in epigastrium, irradiating to the left	7
Muscle rigidity	3
Palpable mass	1

The pain of acute pancreas necrosis is excruciating. One of our own patients, who had just gone through childbirth, stated that this annihilating pain was far worse than anything she had ever experienced. While the radiation to the right upper quadrant and shoulder seem natural in view of the frequent association with gall-stones and common-duct stones, the irradiation to the left, mentioned in seven instances, requires some discussion. Katsch[8] emphasized that irradiation to the left in a gall-bladder colic is suggestive of pancreatic involvement. When one realizes that most of the gland lies to the left of the mid-line, an involvement of the body or tail of the pancreas may easily give such irradiation. It is probable that on careful questioning such a symptom and the occurrence of Head-zones on left-sided segments could be more often elicited.

Jaundice in twelve cases shows that obstruction of bile flow may frequently complicate the picture. Common-duct stone, cholangitis or a swelling of the head of the pancreas are the most commonly quoted causes. However, one must consider the possibility of a toxic hepatitis, a fatty degeneration of the liver or even an acute liver atrophy, as observed in one case of the present series. The serious general intoxication that follows autolysis of the pancreas may be responsible for the hepatic damage. Wolfer[9] has recently summarized and advanced new evidence of a possibility of pancreatic digestion of the biliary tract and liver substance through a backflow of pancreatic enzymes into the common duct in the etiology of certain types of cholecystitis. Whether such a mechanism could also operate during an attack of acute necrosis of the pancreas has not yet been investigated.[10] At present, the hepatic injury can be best explained by the severe intoxication with protein-split products or an ascending pylephlebitis. Uræmia in connection with hepatic damage has been reported,[11,12] and is part of the general intoxication in severe jaundice.

Muscle rigidity does not belong to the typical picture of acute necrosis of the pancreas. In all three cases of our series a diffuse, purulent peritonitis was present. Thus it must be considered as a late sign of serious prognostic value.

A palpable mass in the epigastrium was noted in one case. In thin individuals, with a gastroptosis, the normal pancreas can be palpated at times; swelling, or induration in such a patient, can be palpated a few hours after the onset. Usually, however, the gastric and colonic distention, which is an almost constant symptom of retroperitoneal exudates or hæmorrhages, prevents the palpation of any mass.

Laboratory Examinations.—Blood counts.—(Table IV.) Red blood counts above 5,000,000 were obtained in nine cases. The hemoglobin was correspondingly high. The counts were all taken on entrance to the hospital. The first seven cases were obviously dehydrated, had not taken enough fluids while being sick at home. These high counts would indicate the necessity of parenteral administration of fluids on entrance to the hospital. The last two cases with unusually high red counts must have been both in shock. Case XXIV entered the hospital in the middle of the night with a red count of 7,000,000. Next morning the count was 5,900,000. She was operated on the third day of her entrance and recovered. Case XXX entered the hospital with a count of 8,300,000 and a hemoglobin of 140 per cent., in "agony." The patient was operated on twelve hours after the onset of the attack and died forty-eight hours later. Twenty-four hours after the operation the red count was 5,650,000, with 94 per cent. hemoglobin. The value of interpreting these high red counts as an index of shock has not been utilized in pancreatic surgery. The difference between capillary and venous red cell counts should be a good estimate of the amount of shock,[13] and should certainly warn against immediate operation.

TABLE IV

Red Cell Counts Over 5,000,000 in Acute Pancreatic Necrosis

Case No.	Red cell count	Hemoglobin	Remarks
1	5,500,000	80	Vomited for three days
3	5,700,000	100	Nauseated—nothing by mouth for three days
4	5,208,000	100	No food or liquids for five days
14	5,400,000	70	Sick at home for nineteen days
16	5,650,000	98	Vomited for four days
20	5,440,000	95	Pyloric stenosis
21	5,400,000	90	Vomiting three days
24	7,000,000	?	Five hours after onset
30	8,300,000	140	In shock, ten hours after onset

An unusually low red count (2,230,000, with 55 per cent. hemoglobin) was obtained in Case VII, a deeply jaundiced patient, who died forty hours after the operation. Post-mortem revealed an acute yellow atrophy of the liver.

The other patients showed a moderate secondary anæmia, which is well explained by an elevated temperature, the chronic toxæmia and the fact that they had overcome the initial dehydration.

White Counts.—(Table V.) Leucocyte counts are available in every case and show a great deal of variation. The value of white counts in acute abdominal conditions is probably over-emphasized. So many factors, such as infection, hæmorrhage, shock, dehydration, influence it, so that it can be used only as supportive or additional evidence in diagnosis. Even acute pain produces a leucocytosis.[14] Nevertheless, in this small series it is obvious that white counts below 15,000 were observed either in patients with diffuse peritonitis, whose counts were 3,800 and 4,700 respectively, or in patients with late sequelæ of acute necrosis, such as cysts or chronic pancreatitis. It seems that all cases in the acute stage had a white count above 15,000 and that there were four cases with a count of over 30,000. Two of these patients had a fulminating gangrene and died, while two had late pancreatic abscesses and recovered.

TABLE V

Leucocyte Counts in Acute Pancreatic Necrosis and Its Sequelæ

White Count	Number of Cases	Remarks		
Below 5,000	4	Diffuse peritonitis	2	
		Chronic pancreatitis	2	
5,000–10,000	5	Chronic pancreatitis	3	
		Pancreatic cyst	2	
10,000–15,000	2	Chronic pancreatitis	2	
15,000–20,000	8	Subacute cases	6	
		Terminal in shock	2	
20,000–30,000	4	Acute biliary infection	2	
		Acute pancreatic necrosis	2	
Above 30,000	4	Hyperacute necrosis	2	(both died)
		Abscess of the pancreas	2	

Differential white counts were made in eight patients, three of which showed a neutrophil polymorphonuclear count of over 85 per cent. The differential white count, including the Schilling-Arneth count, has been studied by some authors.[15, 16] The shifting of the leucocytes to the immature forms seems a constant finding but is not specific and is found in any acute destructive process. Its prognostic value has been repeatedly emphasized by Schilling[17]; but only a few of our clinical technicians are trained to use it and its use has not become general.

Examination of the Urine.—Abnormal findings are listed in Table VI. The severe intoxication is again manifested by the frequent appearance of albumen and casts. The occurrence of glycosuria in four cases indicated a disturbance of the internal pancreatic secretion, although it is known that diffuse peritonitis may also produce it. Aceton and diacetic acid were found twice but probably were not determined in every case.

TABLE VI

Urinary Findings in Acute Pancreatic Necrosis

Missing reports	4
Negative	2
Albumen	11
Granular and hyalin casts	9
Sugar	4
Aceton plus diacetic acid	2
Red cells	2

Blood Sugar.—Such determinations are available in six cases, and gave the following readings (Table VII): Of the six cases, three were not acute; the other three were taken shortly after the operation and showed an elevation of blood sugar. In not one case was a pre-operative determination made.

TABLE VII

Blood-sugar Determinations in Acute Pancreatic Necrosis and Its Sequelæ

Case No.	Blood Sugar in mgs. per 100cc.	Remarks
2	75	On sixth post-operative day, two days before death
17	95	Chronic pancreatitis; two years after cholecystectomy
20	92.7	Sclerosis of the head of pancreas
23	142	Third post-operative day
26	131.5	Sixth post-operative day
27	220	Two years after acute necrosis Post-hæmorrhagic cyst

Sugar Tolerance.—Only once was this test performed, in Case XXVI. The values were 122, 227, 272 and 219 milligrams per 100 cubic centimetres of blood taken at 0, ½, 1 and 2 hours after the ingestion of 1.75 grams of dextrose per kilogram body weight. The tolerance was determined one week after the operation for an acute necrosis of the pancreas and shows a definitely diabetic curve. A total of 4.93 grams of sugar were excreted in the urine. Later determinations are unfortunately not available.

Examination of Peritoneal Exudate or Content of Cysts.—In Case X, which seemed to be a case of chronic fat necrosis with a large and quickly refilling peritoneal exudate and no history of acute attack in the chart, the fluid contained bile, 10 per cent. albumin (due to blood) and cultures were negative. In Case XXII, fluid aspirated from an œdematous pancreas revealed pseudo-diphtheroid bacilli, probably a contamination. Except in those two cases, there is no report of chemical or bacteriological study of the exudate except at autopsy.

In two patients the content of cysts was examined for bacteria and was found sterile in two and four days respectively. No anaërobic cultures were made.

Blood Chemistry.—Aside from the blood-sugar determinations, one re-

FIG. 1.

FIG. 2.

FIG. 1.—Case of G. de Takats. Mrs. E. S., aged forty-five. Recurrent attacks of gall-bladder colic with jaundice. Last attack two weeks ago with marked irradiation to the left. Note the irregularity on the greater curvature, which is permanent, and large duodenal curve. At operation a marked enlargement of the head of the pancreas and perigastric adhesions explained the röntgenological findings.

FIG. 2.—Case of G. de Takats. Th. M., aged thirteen. Abscess of the tail of the pancreas, making an impression high up on the greater curvature. The rigid, mottled appearance of the greater curvature simulates malignancy. The abscess was drained toward the flank.

port is available in Case XX of a non-protein nitrogen of 48.4 (normal 35) and a urea nitrogen of 23.3 (normal 15) milligrams per 100 cubic centimetres of blood. This patient had had an operation for pancreatic cyst thirteen years before and returned because of intermittent duodenal obstruction, which was undoubtedly responsible for the high split products. No such determinations are available in acute necrosis of the pancreas, although they would be undoubtedly high.

X-ray examinations are available in five cases. None of these was taken during an acute attack. In acute attacks, the absence of subdiaphragmatic air may exclude gastroduodenal perforation and reveal intestinal obstruction by the aspect of fluid levels. A flat plate on a portable apparatus should

have a definite value in excluding the most frequent conditions that obscure the diagnosis of pancreatic necrosis. Such a diagnosis by exclusion would be very important in determining the optional time of operation, as will be discussed later.

In the absence of acute abdominal symptoms, when a barium meal can be given, the value of X-ray examinations has been emphasized by Case[18] and others. The irregularity on the greater curvature, a pyloric stenosis, a displacement of the transverse colon downwards and stomach upwards, the exaggeration of the duodenal curve are the most frequently observed signs. A few films of our own series serve to illustrate these. (Figs. 1, 2 and 3.)

Time of Operation.—Most statistics bring convincing proof to the effect that in case of acute pancreatic necrosis immediate operation is necessary and that delay raises mortality. Only quite recently have Nordmann, Walzel and Polya expressed their belief that the operation is not capable of arresting the autolytic process and the absorption of protein-split products. They advise against immediate operation and feel that after sequestration or abscess formation, the patient is in far better condition to stand surgical interference. That light cases may be treated conservatively seems uniformly accepted; the discussion centers around the patients, who show from the beginning a severe intoxication and a beginning peritonitis. Previous to their objections, Archibald[19] advocated deferring operation in hyperacute cases with collapse because such patients would not stand the operative interference.

Our cases, although far too limited in number to allow definite conclusions, throw an interesting light on the subject. Table VIII shows the time of operation related to the onset of acute symptoms. It is realized that statistics of this kind are open to criticism; so much depends on other factors, such as the skill of the operator, the severity of the attack, the type of operation, that the time factor alone may not be decisive. However, the immediate operation (less than twenty-four hours) and the late operation (after three weeks) show the lowest mortality. Operations performed in the interval have a mortality of 50 per cent., which is the usually quoted figure in recent mortality statistics (Table I).

TABLE VIII

Time of Operation Related to Onset of Acute Symptoms

Time	Number of Cases	Number of Deaths
Less than twenty-four hours	4	1–25%
Twenty-four to seventy-two hours	2	1–50%
Three days to a week	3	1–33%
One to two weeks	4	2–50%
Two to three weeks	3	2–66%
More than three weeks	5	1–20%

Patients operated on within the first twenty-four hours or after three weeks (nine cases) have an average mortality of 22 per cent.; patients operated on after twenty-four hours but earlier than three weeks (twelve cases) have a mortality of 50 per cent.

That the hyperacute cases may be in shock and have a high red cell count was shown in Table IV. Operation should certainly be deferred in

such patients. In cases that already show evidence of diffuse peritonitis, waiting for localized abscesses would correspond to Ochsner's principles. There is no evidence on hand to show that drainage of the omental bursa, of the biliary tract or of the peritoneal exudate would in any way influence the spreading of necrosis or the virulence of peritonitis. The fulminating cases seem to die, no matter what treatment is instituted; but Nordmann's two cases[20] would indicate that even seemingly moribund patients may be successfully operated on at a later time.

Operation is then most favorable in the early cases that have an œdema of the pancreas without any other involvement; many of these cases subside on conservative treatment and just which would go on to a progressive destruction is impossible to tell. The crux of the situation, however, is this: Can we, with our present diagnostic ability, be sure that we are really dealing with an acute pancreatic necrosis, and not overlooking another type of acute abdominal emergency where delay is fatal? We feel that with a flat X-ray plate gastroduodenal perforation and intestinal obstruction can be excluded; that high blood sugar and high blood diastase content, in the absence of diffuse peritonitis, points to pancreatic involvement with great emphasis. In such patients delay is permissible and may be life-saving; but if in doubt, a rapid exploration is seriously to be considered, if the patient can be brought out of the initial shock.

It is unwise to attempt to lay down hard-and-fast rules for the time of operation, as every case presents a different problem. However, the following principles seem logical to follow.

(1) Never operate on a patient in the initial shock.

(2) If all diagnostic measures point to pancreatic necrosis, delay is permissible, until abscesses localize, cysts or gangrenous parts need removal.

(3) If the diagnosis is uncertain, early operation must be done for fear of overlooking intestinal (appendix) perforation.

(4) If the attack is mild, wait for recovery and then diagnose and operate for biliary-tract infection.

Pre-operative Diagnosis.—Table IX shows the pre-operative diagnosis, as listed on the charts. From this table it is apparent that a diagnosis of acute pancreatic necrosis was not made in one single instance. It is naturally possible that the attending men might have considered such a possibility, but as most hospitals do not require a pre-operative diagnosis from the surgeon before he operates, the interne's diagnosis may be the only one on the chart. Nevertheless, it illustrates the difficulty of diagnosis unless certain laboratory methods will be used. The diagnosis of acute cholecystitis and of common-duct stone has been made in fifteen out of the twenty-two cases, which is essentially correct, being the etiological factor. The involvement of the biliary tract has been found in eighteen out of the twenty-two cases, which gives an 81.2 per cent. incidence of biliary infection as the primary cause. This corresponds to figures given in larger statistics. The diagnosis of intestinal obstruction has been made twice; vomiting and marked colonic distention

are usually present, the transverse mesocolon is œdematous and a paralytic ileus is always present in such sudden retroperitoneal accumulations of fluid. Whether it is ever possible to differentiate this from a mechanic obstruction in the left half of the colon cannot be stated. In such patients, with shock and a low blood-pressure, the use of spinal or splanchnic anæsthesia for diagnostic purposes would not be advisable. Hypertonic sodium chloride solutions overcome paralytic ileus astonishingly well[21] and could be tried. The most important point, however, in ruling out the erroneous diagnoses is the attempt to make a positive diagnosis of acute necrosis of the pancreas by the high fasting blood sugar and high diastase content of the blood. There is only one condition which clinically simulates acute pancreatic necrosis and produces the same laboratory data, and that is a diffuse purulent peritonitis. Unless an appendix-peritonitis or a ruptured ectopic pregnancy can be definitely ruled out, such a possibility must always be kept in mind. The flat X-ray plate will help to diagnose a ruptured viscus by the accumulation of air and the disappearance of liver dullness.

TABLE IX

Pre-operative Diagnosis

In Case of Acute Necrosis		*In Case of Late Sequelæ*		
Acute cholecystitis	12	Pancreatic cyst	2	Correct
Common-duct stone	3	Pyloric obstruction due to previously drained cyst	1	Correct
Intestinal obstruction	2	Carcinoma of pancreas	1	Erroneous
Post-operative ileus	1	Intestinal obstruction	2	Erroneous
Perforated gastric ulcer	1	Tuberculous peritonitis	1	Erroneous
Ruptured appendix	1	Hepatic cirrhosis with ascites	1	Erroneous
Ruptured ectopic pregnancy	1			
Acute cardiac decompensation	1			
	22		8	

In the late cases, a correct diagnosis has been made in three out of eight instances. These diagnoses were made chiefly possible by the use of a barium meal. In the other cases, the hard nedular pancreatitis, that may follow acute necrosis, gave rise to the diagnosis of carcinoma of the head of the pancreas in one instance. A differentiation of these two conditions may not be possible even on exploration. A biopsy of the inflamed pancreatic tissue is listed as one of the possible causes of acute pancreatic necrosis by Schmieden and Sebening.[4] Peripancreatic adhesions and infiltrated omental tags may produce intestinal obstruction. One of us has seen an abscess in the tail of the pancreas, which produced an obstruction at the splenic flexure. Thus the diagnosis of intestinal obstruction as one of the late sequelæ of acute pancreatic necrosis must be considered and cannot be listed as a diagnostic error. The diagnosis of tuberculous peritonitis and of hepatic cirrhosis with ascites has been made. This is due to the appearance of a large peritoneal exudate in some of the late cases of pancreatic necrosis, where large areas of fat necrosis, thickening of the omentum and infiltration of the mesocolon testify to the origin of this disease. The palpable masses

in the omentum may very easily suggest tuberculous peritonitis, whereas the rapid refilling of peritoneal exudate and perhaps a palpable small liver may suggest portal cirrhosis. That the liver is frequently damaged in acute pancreatic necrosis has already been mentioned and will be discussed later.

Findings at Operation.—Table X indicates the findings at operation, related to mortality. When we compare this table with Table VIII, which deals with the time-factor as related to mortality, we find that early operation (less than twenty-four hours) and early anatomical findings (œdema or hæmorrhagic exudate without necrosis) will give the lowest mortality. Provided the patient is not in shock or can be brought out of it in a few hours, this seems the most logical procedure, although some of these patients would probably recover without an operation. On the other hand, patients with certain pathological findings such as acute liver insufficiency and diffuse peritonitis cannot be benefited by an immediate operation, but probably harmed. Abscess or gangrene, when the patient has overcome the spread of infectious or destructive process, do better when opened late. Post-operative pancreatic necrosis, which occurred after operations on the gastroduodenum or biliary tract, proved fatal in all cases. Here the complication was not recognized, the patient was already weakened by the previous operation and the digestion of ligatures and sutures by pancreatic enzymes played a decisive rôle in the fatal outcome.

TABLE X

Main Pathological Findings at Operations for Acute Pancreatic Necrosis

Findings	Number of Cases	Mortality	
Œdema without necrosis	..	..	
Œdema with fat necrosis	1	..	
Sclerosis with fat necrosis	2	..	
Cyst with fat necrosis	2	..	
Hæmorrhagic exudate	7	1	
	12	1	8.3%
Abscess or gangrene	5	2	
Acute hepatic injury	1	1	
Diffuse peritonitis	1	1	
Post-operative pancreatic necrosis	3	3	
	10	7	70%
Total cases	22	8	36.3%

This table, although the number of cases is small, would again urge operation early, when shock is absent. If, however, the patient is seen at a later stage, expectant waiting is advisable. It is true that some patients will die in this interval, but the number of surgical deaths will be higher. An adequate control-series has not been forthcoming and is very difficult to obtain in clinical cases.

The absence of early œdema without fat necrosis in the operative findings would indicate that the diagnosis has not been made so early or that indica-

tion for surgery was not deemed to be present in this series. In several statistics, [4, 7, 22] patients have been operated on with acute œdema of the pancreas and no other findings with a low mortality. Whether they would have recovered without an operation or gone on to progressive destruction, no one can tell at the onset. Hence again, a very early operation should be postulated.

Surgical Procedures in the Treatment of Pancreatic Necrosis and Its Sequelæ.—The grouping of operations as shown in Table XI may seem arbitrary and the mortality figures not conclusive, as so much depends on the pathological findings. However, the first group with minimal interference shows a comparatively low mortality in spite of the fact that some of the most advanced cases are included in it; whereas the second group, with attempts at drainage of the general peritoneal cavity or extensive surgery on the biliary tract, shows a high mortality. Finally, the third group includes operations for late sequelæ, with no mortality in the three cases.

TABLE XI

Surgical Procedures in the Treatment of Acute Pancreatic Necrosis and Its Sequelæ

Type of Operation	Number of Cases	Mortality	
Exploratory laparotomy, no drainage	2	..	
Cholecystotomy	1	..	
Cholecystectomy	2	..	
Drainage of lesser sack	3	1	
Cholecystotomy plus drainage of lesser sack	*3*	*1*	18%
Cholecystotomy plus drainage of peritoneum	7	5	
Cholecystectomy plus drainage of lesser sack	1	1	
Cholecystectomy plus drainage of common duct	*1*	*1*	77.7%
Gastroenterostomy for pyloric obstruction	1	..	
Drainage of pancreatic cyst	1	..	
Drainage of abscess	1	..	0%

The object of any surgical interference in acute pancreatic necrosis is first of all to drain the infected biliary tract, if that is the primary cause of the disease. Such was the case in over 80 per cent. of this series and is probably even higher if special attention is focused on this source. The drainage of the gall-bladder is the simplest and most rapid form of drainage. While cholecystectomy and common-duct drainage would be the ideal procedure and could be done in patients at an early stage of the disease by skilled surgeons, most patients may not stand so much at the time of acute pancreatic necrosis and should have just as little done as possible. The drainage of the omental bursa and the capsule of the pancreas if it is filled with exudate can do no harm and decompresses the gland. The drainage of the peritoneal cavity is useless and impossible. While arguments are still unsettled as to whether the peritoneal fluid is toxic or protective, it seems to be sterile in the early cases. Later, when permeability changes occur, a diffuse purulent peritonitis is present, containing the flora of the intestinal canal. In either case, drainage is of no avail.

Incision of the capsule or even liberation of the gangrenous portion by the gloved finger has been practiced by many Continental surgeons. Walzel[23] has reported a rupture of the splenic vein following such a procedure, which led to a fatal hæmorrhage and warns of any incisions into the parenchyma itself.

It is interesting to note that a simple exploration, during which the condition was not recognized but where tissue taken for biopsy revealed fat-necrosis, has led to recovery in two instances. This confirms our opinion of spontaneous recovery even in the presence of a large peritoneal exudate.

On the basis of these figures and convincing reports of Nordmann, Heller and others, we would emphasize *biliary drainage* before anything else is done, if infection or stones are recognizable. In case of a large retroperitoneal œdema, this could be drained toward the flank. There is no way of preventing progressive necrosis and intraglandular manipulations may do more harm than good. As secondary operations, removal of the gall-bladder, opening of pancreatic abscesses, removal of sequestrated glands, overcoming pyloric or intestinal obstructions may be done with comparative safety.

Complicating Factors and Their Influence on Mortality.—Table XII lists the complications encountered and diagnosed. Pancreatic asthenia is not listed.[24] The association of parotitis and pancreatitis has been the subject of a great many discussions. We refer to the article of Schmieden and Voss.[25] As following other laparotomies, its appearance is an ominous prognostic sign. The thrombosis of the portal vein or its tributary, the splenic vein, has occurred twice, a portal hypertension with ascites twice. This is not surprising, when one realizes the fulminating destruction of tissue that occurs in the area these veins supply. Surgery is helpless in such a complication. An acute swelling of the liver was seen once during operation. This subject has been thoroughly discussed recently by Henschen,[26] although not in connection with pancreatic disease. It calls for biliary drainage perhaps even through hepatic parenchyma. Our one case recovered.

TABLE XII

Complicating Factors and Their Influence on Mortality of Acute Pancreatic Necrosis

Complications	Number of Cases	Deaths	
Bilateral parotitis	1	1	
Thrombosis of splenic vein	1	1	
Portal thrombosis with infarct	1	1	
Portal cirrhosis with ascites	2	2	
Toxic hepatosis	1	1	
Pleural empyæma	1	..	
Subphrenic abscess	1	..	
Nephrosis with anuria	1	1	
Total complications	9	7	77.7%

Pleural empyæma and subphrenic abscess are not infrequently seen as a late complication. Their adequate drainage resulted in cure. One patient died of an acute kidney-insufficiency with complete anuria. We have referred

to this complication as a sequel to hepatic injury. It is probably part of the general toxæmia.

The Total Mortality Rate.—Of the thirty patients, eleven died, thus giving a mortality of 36.6 per cent. Eight patients were operated on for late sequelæ, which leaves twenty-two cases of acute pancreatic necrosis with eight deaths, a mortality of 36.6 per cent. This is surprisingly less than the statistics shown in the first table, which vary around 50 per cent. It is pos-

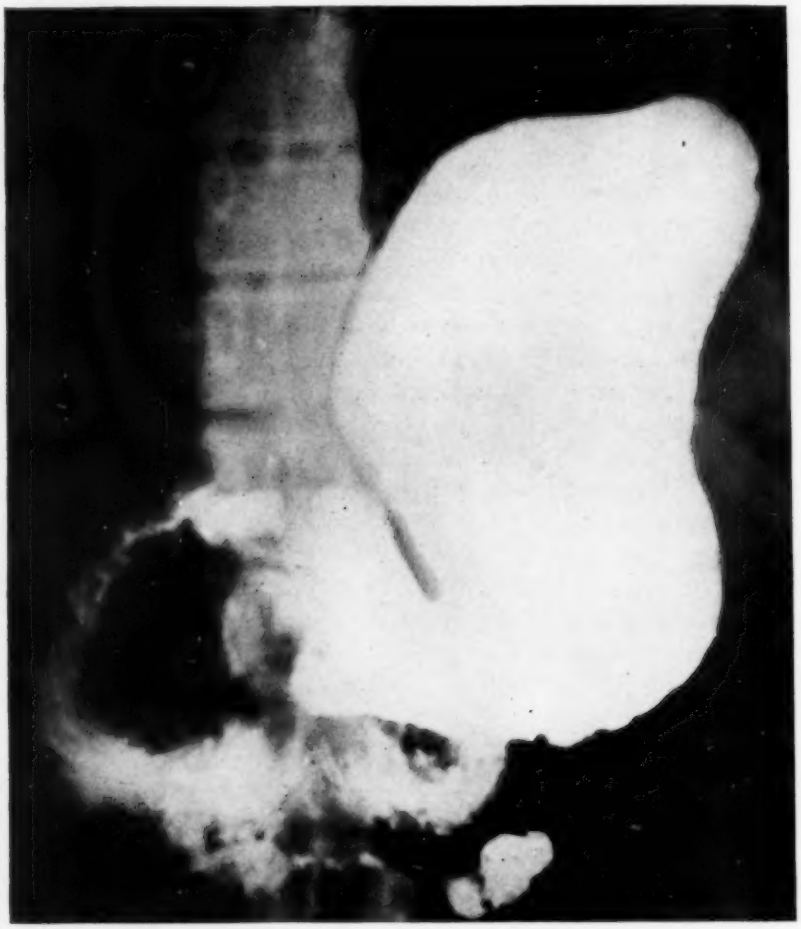

FIG. 3.—Case of G. de Takats. Mrs. E. C. The stomach is large, deformed and empties slowly. The pyloric half of the stomach, on the greater curvature, is displaced upward and toward the left. The duodenal curve is spread out over a larger area than usual. The stomach empties in eight hours. (Report of Dr. J. T. Case.) This was a case of a huge pancreatic cyst, involving the head and body of the pancreas with marked perigastric adhesions. The suture of the cyst wall to the abdominal wall produced a partial pyloric obstruction.

sible that the delay in operating on these non-diagnosed cases unintentionally improved the surgical risk. Also, the frequent use of biliary drainage without any operations on the pancreas, whose involvement has not been suspected at the time of operation, may have improved the statistics. Thus of the twenty-two cases only four came to operation within the first twenty-four hours; whereas in Jung's statistics (*cit.* Guleke[3]) nine out of nineteen, in

Stephan's material four out of eleven and in Zoepffel's cases four out of fourteen came to operation within the first twenty-four hours. Curiously enough, these statistics were compiled to prove that early operation improves the mortality. A glance at Zoepffel's table indicates exactly the same findings that we have arrived at, but interpreted differently: namely, that if the patient is not seen and operated on within the first twenty-four hours, the operation should be deferred to a later period of localizing symptoms. The fact that so many patients die if operated on after twenty-four hours was interpreted as a proof for earlier operation. We are thoroughly in agreement with those who postulate early operation, in the stage of œdema. If, however, necrosis is present, if the patient is first seen three or four days after the acute onset, then conservative treatment, at least for the time being, appeals more to us.

Late Sequelæ of Acute Pancreatic Necrosis.—The patient, who has once gone through an attack of acute pancreatic necrosis, is not safe from late complications. Table XIII lists only one case of recurrent attack, which would be about 4 per cent. of all acute attacks. In reëxamining a number of patients, we frequently hear of recurring epigastric pain, indigestion, nausea and distention. If the biliary-tract infection had been the primary cause, and only an emergency cholecystotomy was done, these recurrent mild attacks indicate a cholecystectomy, and, if necessary, a common-duct drainage. Another cause for recurrent symptoms which requires operation is late sequestration of gangrenous pancreatic tissue, which may have to be removed years after the first operation. The appearance of a persistent pancreatic fistula, with its digestive action on the skin, also needs surgical interference, if it does not close spontaneously in about six months. It may be due to small gangrenous patches of glandular tissue or to a secreting true cyst, whose endothelial lining has not been destroyed. Hohlbaum[27] implanted the secreting pancreatic stump or the wall of the cyst into an upper jejunal loop in three patients. This method deserves serious consideration in suitable cases.

TABLE XIII

Late Sequelæ of Acute Pancreatic Necrosis

	Number of Cases
Recurrent mild attacks	1
Recurrent acute necrosis	1
Persistent fistula	1
Sclerosis of the pancreas	1
Pancreatic cyst	2
Pyloric stenosis following drainage of cyst	2
Diabetes	2
Incisional hernia (6 cases examined)	5

A sclerosis of the pancreas is listed in one case, which had been explored two years after the original attack. There are usually marked digestive disturbances present and a prolonged common-duct drainage or a splitting of the pancreatic capsule, as advocated by Payr and Martina,[28] seem indicated.

No such operations were performed in this series. The operation is not entirely without danger, as acute necrosis and pancreatic fistula may develop after splitting of the adherent capsule.

A pyloric stenosis developed in two cases following suture of the cyst wall to the peritoneum. One patient had a gastroenterostomy, while the other had only a slight intermittent attack of obstruction, although there was a large eight-hour residue of barium. (Fig. 3.) This observation would warn us not to resect too much of the cyst wall in future, as too much tension of the cyst when sutured to the abdominal wall may obstruct the pylorus or cause a marked distortion of the stomach. Two pancreatic cysts have been operated on; both were peripancreatic pseudo-cysts, the results of a previous hæmorrhagic exudate in the omental bursa. A case observed by one of us (de T.) had an acute pancreatic necrosis right after childbirth. The gall-bladder was drained by the obstetrician with the diagnosis of an acute cholecystitis and the pancreas not explored. She was first seen and operated on by us two years later for a large peripancreatic cyst.

Diabetes developed in two cases that have been known to be sugar-free before the acute necrosis set in. This would correspond to almost 10 per cent. of all cases. That latent disturbances of carbohydrate metabolism exist in a larger percentage of cases has recently been frequently discussed.[29]

We were able to obtain post-operative sugar tolerance curves on four other patients, two of which showed abnormally high curves (Chart I). Naturally, the time elapsed since the operation is an important factor, since the great regenerative power of the pancreas, particularly in younger individuals, may overcome even quite serious loss of pancreatic tissue.[30] In older individuals, or in patients who develop a chronic pancreatic sclerosis following acute necrosis with fatty diarrhœa, a decrease in sugar tolerance should be looked for.

One patient had attacks of fatty diarrhœa which could promptly be controlled with tablets of pancreatic extract.

Five out of six patients had an incisional hernia at the site of drainage.

Autopsy Records.—Death occurred in eleven out of thirty cases, a mortality of 36.6 per cent. Of the eleven deaths, seven came to autopsy. The main findings are listed in Table XIV. Pancreatic necrosis was naturally present in all cases as evidenced by gangrenous masses in the gland and fat necrosis spreading through the mesocolon, omentum and not infrequently in perirenal tissue. Its chief spread is through the lymphatics. The peculiar blotchy, lattice-like cyanosis, that is not infrequently present during life, is an important diagnostic sign, according to Walzel,[31] and does not disappear after death. One of us (de T.) has repeatedly seen it on the autopsy table. Its mechanism has never been explained although a stasis of the superficial abdominal veins, accentuated by a sudden increase of pressure in the vena cava, is a possible explanation. There is no fat necrosis in the abdominal wall, but the subcutaneous fat is frequently pale and œdematous.

TABLE XIV

Autopsy Records

Main Pathological Findings in Seven Cases

Findings	Number of Cases	Findings	Number of Cases
Pancreatic necrosis	7	Sero-fibrinous peritonitis	2
Cholelithiasis	4	Purulent peritonitis	2
Common-duct stone	2	Thrombosis of splenic vein	1
Acute cholangitis	1	Portal thrombosis	1
Focal liver necrosis	2	Pleural empyæma	1
Fatty degeneration of the liver	1	General septicæmia	1
Acute yellow atrophy	1	Hæmorrhage into adrenal gland	1

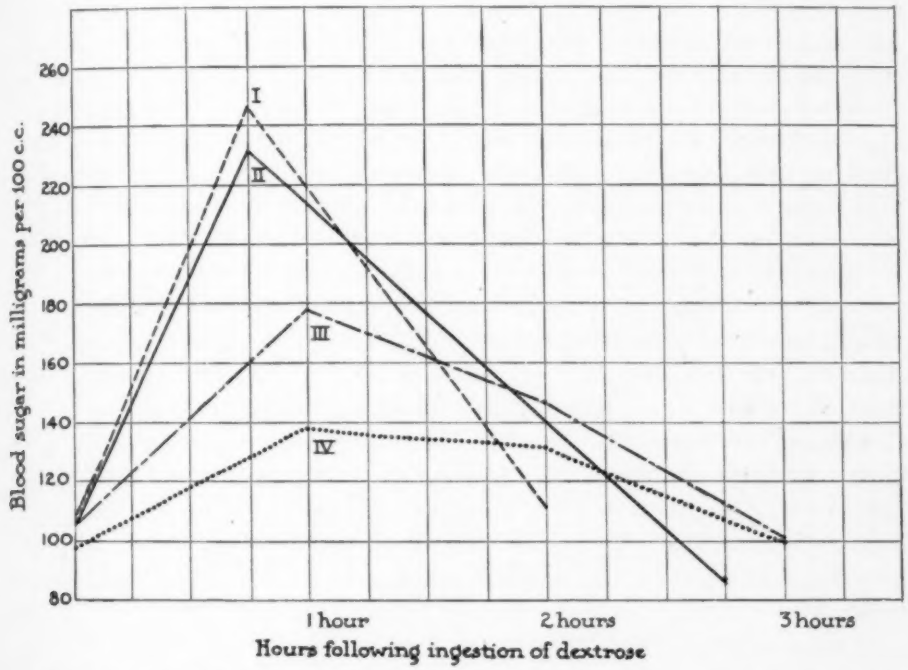

CHART 1.—Sugar-tolerance curves in four patients several years after acute pancreatic necrosis. Cases I and II had fifty grams of dextrose in 25 per cent. solution, and samples of finger-blood were taken at forty-five minutes and two hours. Cases III and IV received 100 grams of dextrose and samples were taken at one, two and three hours. The four curves, then, are not entirely comparable. Nevertheless, it is obvious that the first two patients, in spite of the smaller amount of dextrose, showed a very sharp rise of blood sugar, whereas the latter two show normal peaks. None of these curves can be called diabetic, but the sharp initial rise is suggestive of poor glycogen fixation in the liver and has been seen in mild diabetic cases. (Noorden and Isaac: Die Zuckerkrankheit und ihre Behandlung. Eighth Edition, p. 157, Julius Springer, Berlin, 1927.) The slow fall in Cases III and IV may be due to their age. Case I.—Mrs. J. M., aged forty-eight, six years after operation. Case II.—Mrs. E. G., aged forty-four, seven years after operation. Case III.—Mrs. M. W., aged seventy, seven years after operation. Case IV.—Miss J. J., aged fifty-two, two years after operation.

The high incidence of gall-stones, common-duct stones and biliary-tract infections corresponds to the findings on the operating table. Attention should be drawn to the occurrence of liver damage, which may be the immediate cause of death by hepatic insufficiency.

Peritonitis has been noted in four cases. The exudate is first sterile and later becomes infected by the intestinal flora. The two sero-fibrinous exu-

dates have not been cultured, one of the purulent exudates yielded *B. coli* and anaërobic Gram-positive cocci and bacilli and Gram-negative bacilli. In Brütt's series,[32] the peritoneal exudate was sterile in twelve out of seventeen cases, two showed *B. coli* and three staphylococci. Liver and pancreas were sterile in 64 and 50 per cent. respectively, the rest showed aërobic and anaërobic bacteria. This is of great interest because of Dragsted's[33] work on the importance of anaërobic bacteria in the toxicity of autolytic products. That a sudden gangrene of the pancreas would serve as an excellent medium for previously dormant bacteria is very suggestive, and would explain the rôle of infection in acute pancreatic necrosis. Another source may very easily be the intestinal canal, where permeability changes, probably due to bile-salts, would result in an invasion of bacteria into the peritoneal exudate, as postulated by Andrews.[34] Whether these experimental findings are applicable in man can be settled only by a routine and reliable bacteriological study of exudates found in acute pancreatic necrosis.

Thrombosis of the splenic vein and portal thrombosis have been found once each, but not in the same case. It is surprising that this complication does not occur more frequently, in the presence of such massive, and probably infected tissue destruction. Pleural empyæma was found once. Clinically, one sees not infrequently an immobility of the diaphragm, mostly on the left side, with a serous pleural exudate above it. This accompanies the retroperitoneal and subdiaphragmatic œdema, and through the extensive lymphatic connections through the diaphragm, may easily become infected. Together with subphrenic and perinephritic abscesses pleural empyæma must always be looked for as a complication of acute pancreatic necrosis.

General septicæmia was the cause of death in one case, originating in a diffuse purulent peritonitis. An adrenal hæmorrhage on the left side is noted once. Whether this occurred as an extension of a hæmorrhagic pancreatitis from the tail of the pancreas, or whether it occurred as a terminal phenomenon, cannot be determined from the record. It is, of course, known to occur in virulent infectious diseases with a fatal outcome, and could be clinically suspected by a hypoglycæmia.

Discussion.—*The Pre-operative Diagnosis.*—The difficulty of diagnosis was best illustrated by Table IX, from which it would seem that a positive diagnosis has not been made (at least on the chart) in one single instance. As a routine procedure, not requiring much loss of time or special laboratory facilities, we would recommend the following measures in abdominal emergencies, when pancreatic necrosis is suspected.

(1) *Complete Blood Count.*—High red cell count and hemoglobin mean either dehydration, or, if the attack is hyperacute, gives the degree of shock. High white count rather speaks for acute localized inflammatory reaction; if it is unusually low, and rigidity is present, it is suggestive of peritonitis. High percentage of polymorphonuclear neutrophils signifies the virulence of acute infection. The Schilling-Arneth count will probably not be available

in most hospitals and can certainly not be counted on in emergencies during the night.

(2) *The urine specimen* contains albumen and casts in almost all acute abdominal cases, but the appearance of sugar is suggestive of pancreatic disease. However, it was only present in four out of twenty-two cases, and its absence is certainly not proof against pancreatic necrosis.

(3) *A Blood-sugar Determination.*—A high fasting blood sugar, according to the extensive studies of Krotoske[35] is present in acute pancreatic necrosis. Only a diffuse purulent peritonitis will give such high figures and if that can be eliminated with fair certainty the diagnosis of acute pancreatic necrosis is certain. The figures must be above 160 milligrams to be of any value as smaller elevations might be present with other acute suppurative conditions. We consider a blood-sugar reading, which can be taken by any of the newer micro methods, as the most important aid to a positive diagnosis.

(4) *The Determination of Diastase in Urine and Blood.*—Much has been written recently of the value of diastase determinations in acute pancreatic disease. We refer to only one comprehensive article by Skoog,[36] who made about 3,000 diastase determinations on acute abdominal cases. He determined urinary diastase and felt that while increased values may occur, although seldom, in other acute abdominal conditions, a negative finding, provided the determination is made within twenty-four to thirty-six hours after the onset of symptoms, *excludes any pancreatic pathology.* One of us, with Nathanson,[37] studied the rise in blood diastase following ligation of the tail of the pancreas. The original Wohlgemuth test,[38] modified for clinical purposes, is so simple to run that internes not trained in laboratory work can use it. It is far easier to determine than blood sugar. Because most clinical laboratories are unfamiliar with this test and its value in pancreatic disease, a brief description follows:

Ten cubic centimetres of blood are taken from a vein in a centrifuge tube, allowed to clot and gently centrifuged. Ten test tubes are set up in a rack. One cubic centimetre of serum (or urine) is pipetted into the first and second tubes. One cubic centimetre of 1 per cent. sodium chloride is pipetted into all ten test tubes. After proper mixing of serum and sodium chloride in tube 2, one cubic centimetre is pipetted over into tube 3. Here again, after proper mixing, one cubic centimetre is pipetted into tube 4 and so on up to the tenth tube. The last cubic centimetre pipetted out of the tenth tube is discarded. To every tube two cubic centimetres of a 0.1 per cent. soluble starch solution (Kahlbaum) are added, well mixed, and the whole rack of tubes incubated in a thermostat at 38° C. for thirty minutes. Thus the starch-splitting ferment of the blood can act on the starch solution. At the end of thirty minutes, the fermentation is abruptly stopped by immersion of the tubes in cold water for a few minutes. Three drops of a fiftieth normal iodine solution are added to each tube. The undigested amylodextrin gives a blue reaction, the erythrodextrin red, and the achrodextrin yellow. The end point is read at the tube which shows the first trace of purple without being a solid blue. Suppose this occurs in the fourth

tube. The quantity of diastase in the serum, which was able to digest starch up to that dilution, is calculated as follows: $D=2^4=16\ \frac{38}{30}°$ indicating at the same time the temperature and duration of the incubation. Values between 16 and 32 are normal with this technic. Following experimental duct ligation the diastase has risen to values between 1024 and 3072, which shows the enormous quantities of ferment that can be flooded into the blood-stream when external secretion is obstructed.

We are perfectly aware of the fact that the figures obtained in this manner could be made more accurate. The fact that the serum is incubated

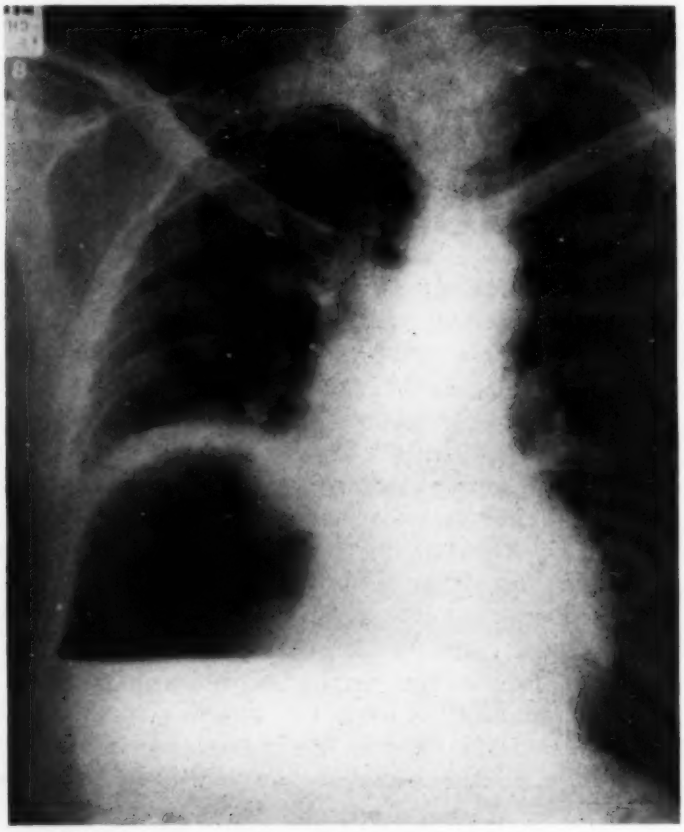

FIG. 4.—Mr. E. C., aged forty-eight. Five days after onset of excruciating pain in upper abdomen, shock, cyanosis, no rigidity. On entrance to the hospital, this large gas bubble was found under the right diaphragm, above a fluid level. The subphrenic abscess was due to a perforation of an ulcer on the lesser curvature. Case of Drs. W. H. Nadler and G. de Takats.

only for thirty minutes and that the starch solution is not buffered to the optimal p_h of diastatic action (7.2) inhibits the action of the ferment. However, the rapidity and simplicity of the test described above makes it possible to use it anywhere, even in the middle of the night, provided the few necessary reagents are ready for use. It is, of course, possible, as Wohlgemuth more recently suggested,[39] to have a starch solution buffered with sodium phosphate to a p_h of 7.2 and to accelerate incubation to fifteen minutes by

using a water bath of 45° C., but we still feel that the test, as described above, serves the purpose of a rapid and adequately reliable orientation.

(5) *Röntgenological Examination.*—In spite of the valuable information that can be gained in obscure abdominal emergencies by films taken by portable X-ray apparatus, such examinations are not carried out often enough. Case,[40] since 1911, has repeatedly emphasized the value of such studies in acute intestinal obstructions, particularly those following operations. An opaque medium is not necessary and the patient is very little disturbed. Laurell[41] has summarized his vast experience with the interpretation of flat films in intestinal obstruction, diffuse peritonitis and localized abscesses. Concerning acute pancreatic necrosis, he believes that a dilatation of the transverse colon and retroperitoneal thickening in the fatty tissue are suggestive, together with a sluggish diaphragm on the left side and exudates in the pleural cavity. A few spoonfuls of barium may bring out the changed contours of duodenal mucosa, and possibly duodenal displacement. Abscesses in the omental bursa can be well visualized.

We have no experience with the positive value of portable X-ray films in a case of acute pancreatic necrosis; however, as a method of excluding mechanical obstruction to the bowel, or gastroduodenal perforation with the characteristic subdiaphragmatic air bubble (Fig. 4) as emphasized by Schnitzler, Vaughan and Singer, its great value is obvious. It may also reveal the characteristic picture of localized peritoneal abscesses long before the clinical symptoms would permit of drainage.

To sum up our aids in pre-operative diagnosis: History of previous gall-bladder attacks, sudden sharp, excruciating pain in the epigastrium with frequent irradiation to the left, often nausea and vomiting, no rigidity, but definite tenderness in the epigastrium with ballooning out of the transverse colon, a marked cyanosis, blotchy and streaky in character. If the patient is in shock, the blood-pressure can hardly be taken. The pulse is empty. The temperature in the early cases is not elevated.

The blood count indicates the degree of dehydration and shock, the urine may contain sugar, but the blood sugar is high and so is the diastase content of the blood. The value of the test for diastase and a portable X-ray film are mainly important for their negative findings, whereby pancreatic necrosis can be excluded.

Pre-operative Management.—If the patient is in shock, as evidenced by the blood-pressure reading and the high red cell count, treatment should be instituted against shock. Small doses of morphine, heat, but chiefly a 6 per cent. gum-acacia solution intravenously will raise the blood-pressure very quickly. In cases of post-operative shock we know of no simpler and more efficient method. The purified gum-acacia solutions are kept in 100 cubic centimetre ampules, diluted to 500 cubic centimetres with normal salt and are free of all previous objections to impurities.[42]

The rapid depletion of liver glycogen, the frequency with which liver damage is found at post-mortem, indicate the administration of dextrose and insulin. This should be given slowly, about 100 grams of dextrose in

10 per cent. solution, together with twenty to thirty units of insulin. Nothing should be administered by mouth, and if there is continuous nausea or repeated vomiting, a Rehfuss tube is passed and the stomach aspirated for retained gastric contents.

As discussed under the indications for operation, an early operation, if the patient is not in shock or has come out of shock, has a low mortality. However, most patients come to the surgeon after more than twenty-four hours have elapsed since the acute onset. If a positive diagnosis of acute necrosis can be made an expectant treatment can be instituted. About 3,000 cubic centimetres of fluid must be given daily; if the patient is obviously dehydrated, 4,000 cubic centimetres. Preferably dextrose-Ringer solution, or dextrose normal salt solution with about one unit of insulin to every three grams dextrose is used. Nothing is given by mouth. If there is considerable intestinal paralysis, twenty cubic centimetres of a 10 per cent. solution of sodium chloride will relieve distention. Under such a régime, even moribund patients may be revived and operations deferred to a later time. If patients die during this time with a peritonitis, an anuria or hepatic insufficiency, no operation could have saved them.

Surgical Procedures.—The anæsthesia is preferably gas-oxygen with local anæsthesia of the abdominal wall. Spinal anæsthesia, particularly in the early cases that may just have been in shock, does not seem advisable. The minimal amount of surgery should consist of draining the biliary tract by cholecystostomy and drainage of the omental bursa. A lumbar drainage through the left flank may be seriously considered, as Lotheisen[43] reports a mortality of 18 per cent. since the routine use of a lumbar drain. The mechanical conditions for drainage are more favorable and a post-operative ventral hernia may be thus avoided.

Post-operative Treatment.—Because of the possible injury to internal secretion, all patients should be watched for a decrease in sugar tolerance and suitable dietary restrictions or even insulin should be administered. The patient should be informed of a possibility of recurring attacks, particularly if the biliary-tract infection has not been radically attended to. In six months to a year following complete closure of the wound, a cholecystectomy, and, if necessary, common-duct drainage should be advised and at the same time the incisional hernia, which almost invariably follows pancreatic drainage, can be attended to. Disturbances of external pancreatic secretion can be ameliorated by potent pancreatic extracts given orally. In patients who develop a late pseudo-cyst or a sclerosis of the pancreas, further surgical procedures must be advised.

Summary.—Thirty cases of acute pancreatic necrosis or their sequelæ have been discussed. The uncertainty of pre-operative diagnosis and the high mortality challenge to further efforts in this field. A routine use of blood-sugar and blood-diastase determinations together with a frequent employment of flat X-ray plates may greatly improve our diagnostic ability. The proper time of operation and the selection of the proper surgical methods will diminish mortality. Attention should be focused to late sequelæ of acute

pancreatic necrosis, some of which can be prevented. A prophylaxis of acute pancreatic necrosis for the large majority of cases lies in early surgical treatment of biliary-tract infection.

We wish to express our deep gratitude to the staffs of Evanston and Wesley Memorial Hospitals and particularly to Drs. Charles A. Elliott, William R. Parkes and Harry M. Richter for the privilege of obtaining follow-up records of their patients.

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CHRONIC INTERLOBULAR PANCREATITIS

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The pancreas is the only intra-abdominal organ that produces symptoms of a chronic surgical nature that physical examination, röntgenologic or laboratory studies will not aid in establishing a diagnosis except by negative findings. Of course, when the Islands of Langerhans are diseased we have glycosuria and hyperglycæmia, but chronic infection of the pancreas rarely gives evidence of disturbed carbohydrate metabolism. In considering chronic pancreatitis it is essential to understand the histologic picture of the normal organ which is illustrated in Fig. 1, and one will then have a clearer conception of chronic interlobular pancreatitis. I have studied[6] sections from the pancreas in sixty-six cases to determine whether chronic pancreatitis is a relatively frequent disease. Of these cases fifty were taken from people meeting with accidental death and sixteen from people with acute peritonitis from different causes, and in none was there evidence of chronic pancreatitis.

Etiology.—Chronic pancreatitis is divided into two forms: first, chronic interlobular pancreatitis; and second, chronic interacinar pancreatitis. The interlobular type results from bacteriologic infection of the connective tissue lying between the lobules and it is the one that interests us in this paper. The interacinar pancreatitis is the result of arteriosclerotic changes and is usually associated with diabetes and this bears little or no relation to infection, while chronic interlobular pancreatitis rarely involves the lobules. How infection reaches the pancreas in the chronic type of disease has not been settled, but there is considerable debate as to whether it ascends the ducts, is of a lymphatic origin, or is produced by direct extension from an associated disease, such as duodenal ulcer. Archibald,[1] in 1913, in a paper entitled "A New Factor in the Causation of Pancreatitis" reported thirty-six cases of pancreatitis in 60 per cent. of which gall-stones were absent. He attributes the pancreatitis to a spasm of the sphincter of Oddi at the ampulla, which results in bile entering the pancreatic ducts. Mann and Giordano,[9] working experimentally on goats, doubly ligated the common bile-duct and divided it at its entrance into the duodenum. The animals lived from one to thirty days. In none was there either macroscopically or microscopically an area with the appearance of acute hæmorrhagic pancreatitis. The results of these experiments emphasize: first, that with the pancreatic duct emptying directly into the common bile-duct and the latter completely obstructed, bile was not forced into the pancreas except after a considerable length of time. Second, that bile did pass into the pan-

creatic duct and infiltrated the pancreas completely when under the maximum of pressure which the physiologic mechanism of the animal could produce, but acute hæmorrhagic pancreatitis was not seen.

Sweet,[11] in working experimentally on dogs, has been able to remove a portion of the pancreas and join the head of the pancreas or the duct to the intestine without danger of pancreatitis, either acute or chronic, for as long as an eleven months' interval. From these experiments it would seem that infection rarely ascends the ducts in animals. This may be an explanation for some cases of chronic pancreatitis in humans, but it seems doubtful whether it is the most common cause.

The lymphatic origin of the disease has an abundance of clinical data to support such a contention. Deaver and Pfeiffer[3] report a series of fifty-two cases of chronic pancreatitis in which the head alone was affected in

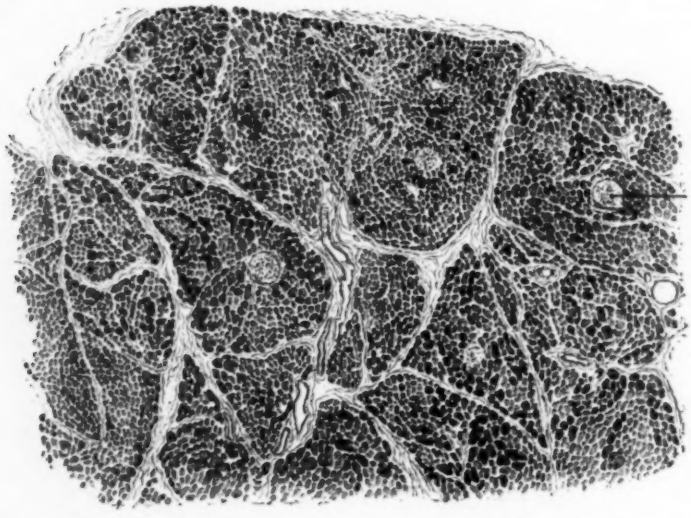

FIG. 1.—Reproduction from Piersol's Histology showing the gland divided into lobules with the interlobular connective tissue.

forty-two and in only nine was the tail involved. In twenty-seven cases there was well-marked evidence of involvement of the lymph-nodes in the neighborhood of the head of the pancreas. They found the infection localized chiefly in the triangle of the pancreatic infection, between the duodenum and converging ducts of Santorini and Wirsung. They attribute the chronic infection to lymphatic origin. If the infection ascends the pancreatic ducts, the induration should be more general. The lymphatics from the gall-bladder drain only to the triangle of pancreatic inflammation, as has been demonstrated by Franke.[5] Of the seventy-nine patients with chronic pancreatitis at the Lankenau Hospital reported by Deaver, seventy-two or 91 per cent. showed evidence of biliary infection, while forty-two or 53 per cent. had calculi.

The following cases will illustrate that chronic interlobular pancreatitis is frequently produced by direct extension from duodenal ulcers.

CASE I.—Male, aged fifty-two years, admitted to the Fourth Surgical Division, Bellevue Hospital, January 26, 1928, having previously been operated upon in another hospital in Greater New York on December 15, 1927. The patient on admission was jaundiced and complained of severe abdominal pain and was receiving morphine grains 1/6, t. i. d. A résumé of the operative findings from the other institution was carcinoma of the head of the pancreas with metatasis to the spine. In view of this diagnosis it was thought advisable to do a gastro-intestinal series to demonstrate the pancreatic tumor, but the patient was found to have a duodenal ulcer from the röntgenologic findings. The patient was put on a Sippy diet and within one week was greatly improved and was taken off morphine, and discharged from the hospital February 12, 1928. He was followed in the Gastro-Enterological Clinic until April 23, when he was readmitted, due to the fact he had been having severe pain for two weeks, but previous to this he had been symptomatically well for two months. Dr. John H. Morris operated upon the patient April 26 and an ulcer was found in the second portion of the duodenum with a large induration of the head of the pancreas the size of a large lemon. A gastro-enterostomy was done, the gall-bladder found normal, the appendix was not removed. The patient has been followed regularly since the operation and has had no complaints referable to his stomach and is symptomatically well.

CASE II.—Male, aged fifty-two years, admitted to the Gastro-Enterological Clinic of the Fourth Medical and Surgical Divisions at Bellevue Hospital January 12, 1929, with a röntgenologic diagnosis of pyloric ulcer. Patient was put on a Sippy diet. He was symtomatically well until September 28, and became X-ray negative June 14. He was also negative October 3. After his symptoms returned the pain could not be relieved by conservative treatment, although his gastro-intestinal series were negative. He was then admitted to the hospital and was operated upon by me November 9, 1929. On opening the abdomen the gall-bladder was found normal, the duodenum was mobile and easily inspected, no evidence of an ulcer was found on the anterior surface but a slightly indurated area was felt posteriorly, and the head of the pancreas was the size of a lemon. A posterior gastroenterostomy was done, and also an appendectomy. The patient made an uneventful recovery. He has been followed regularly in the clinic since that time and has remained symptomatically well and X-ray negative.

CASE III.—Male, aged fifty-seven, seen first January 16, 1931, with a history of a duodenal ulcer for eighteen years. He had been under the care of Dr. Arthur F. Chace for the past fourteen years. He did very well on medical treatment until two years before seen by me. His pain had increased gradually during the previous two years and he did not get relief from diets. The pain was intense enough to keep him awake several hours at night and during the past three months it had increased in severity. A gastro-intestinal series on January 10, by Dr. I. Seth Hirsh, revealed a healed duodenal ulcer and the gall-bladder negative. Doctor Chace felt that this patient should be operated upon and he was referred for same, the pre-operative diagnosis being chronic pancreatitis and duodenal ulcer. At operation the patient was found to have an ulcer in the second portion of the duodenum and the duodenum was adherent to the pancreas, which was the size of a lemon. A posterior gastroenterostomy and an appendectomy were done and the patient has been symptom-free for the past six months.

These cases, besides six others with duodenal ulcers and chronic pancreatitis whom I have seen, will illustrate that chronic pancreatitis may arise by direct extension from associated infections.

From the above data it would seem that the gall-bladder and biliary system are the primary factors in producing chronic infection of the pancreas. Ulcers of the duodenum probably play the second most important rôle, while the appendix and ileocecal angle have direct lymphatic drainage to the head of the pancreas.

Signs and Symptoms.—We are referring to acute exacerbations of upper abdominal pain that occurs in patients following cholecystectomies, or in patients suffering from gastric or duodenal ulcers who have not been operated upon. Pain is the chief complaint of the patient and the individual is usually seized with a severe upper abdominal pain which is constant in character. It is difficult for these patients to localize the pain but occasionally they say it is in the right upper quadrant and radiates to the back. More frequently they state the pain is on the left side in the region of the left kidney, and due to its location on the left side it would make one suspect a renal calculus. The intensity of the pain will vary in different individuals, presumably depending upon the severity of the pancreatic involvement. These attacks may last from a few hours to forty-eight or seventy-two hours. If the pain is located in the left kidney region at the beginning of the attack, it quite frequently localizes itself in the upper abdomen in the middle of the epigastrium after forty-eight hours or so. The patients usually feel normal within a few hours after the pain subsides. Nausea is not commonly seen in this condition. Vomiting is usually encountered and it comes on approximately within the first hour of pain and usually persists during the attacks. The vomitus is clear or slightly bile-tinged and non-offensive. Because of the persistent vomiting and the sudden and severe abdominal pain, one often suspects a high intestinal obstruction, but the general appearance of the patient is not that of one suffering from an intestinal obstruction, and in spite of the great pain and persistent vomiting the general condition does not indicate that the patient is critically ill. Jaundice is quite frequently encountered in the severe cases, particularly after they have been incapacitated for forty-eight or seventy-two hours. This is presumably due to a compression of the bile duct as a result of the swelling of the head of the pancreas. According to Helly[7] the common duct passes through the head of the pancreas in approximately 62 per cent. of cases. Mayo Robson[10] believes that some of the cases of catarrhal jaundice may be due to a mild pancreatitis.

On physical examination the abdomen is usually not distended and does not have any marked rigidity, but the patient complains of indefinite tenderness over both upper quadrants and frequently in the costovertebral angle, more frequently on the left side than the right. Eggers[4] was impressed with the lack of physical signs as compared with the severity of the symptoms in his cases. In two of his patients the house staff ventured to state that they were simply neurotic. The temperature is usually normal, but when elevated it is around 100° F. The blood examination, in the milder cases, will reveal a normal leucocyte count or only a very slight increase in the total count, as well as the polymorphonuclear leucocytes. The urine analysis is negative.

The diagnosis of this condition can be made only by the process of elimination. One must exclude renal calculi and bear in mind the possibility of a stone in the common duct which was overlooked at the original operation. In the severe forms of this condition it is sometimes impossible to

make a diagnosis without an exploratory laparotomy. In the milder types of infection one should suspect the pancreas as the cause of trouble and keep the patient under observation. In Judd and Burden's[8] series, the findings after an exploratory laparotomy were pancreatitis in seventeen out of twenty-four cases, and the common bile-duct was patent in all. Aub and his co-workers[2] have stated, in a recent publication, that 20 cubic centimetres of 5 per cent. solution of calcium chloride administered intravenously will give immediate relief in lead colic and biliary or renal colic, but if the pain is due to cholecystitis without stones, or ulcers of the stomach or duodenum, it is only partly effectual in relieving pain. In view of their observations it would seem that calcium chloride should be of definite value in differentiating between a stone in the common duct and chronic pancreatitis.

Treatment.—A patient suffering from a chronic pancreatitis associated with an ulcer of the stomach or duodenum offers a very excellent prognosis if the ulcer is operated upon. Usually a gastroenterostomy will suffice to give such a patient a symptomatic cure. The seven cases that have been operated upon and are now being followed in the Gastro-Enterological Clinic of the Fourth Medical and Surgical Divisions of Bellevue Hospital are symptomatically well, the longest period since operation being three and a quarter years and the shortest nine months. I have also two cases operated upon in private practice, six or eight months ago, that are symptomatically well. In patients that have had previous laparotomies for cholecystitis and cholelithiasis usually in due course of time, meaning from one to three years, they outgrow their symptoms if a cholecystectomy was done at the original operation as the pancreatic infection in this instance is secondary to the gall-bladder disease which has been removed, and the infection in the pancreas will then subside. Conservative treatment in this type of patient should be employed as further exploration is of no value and probably introduces additional infection.

Comment.—The "flare-up" of symptoms of a chronic pancreatis can be compared to the acute exacerbations of chronic osteomyelitis, meaning that the organ is diseased and unless the primary focus is operated upon the pancreatic infection will become more extensive and even after operations on the biliary tract these exacerbations will occur, which is one reason for not allowing a patient to go over a prolonged period with a chronic cholecystitis that does not respond to medical treatment. The chronic infections and the acute exacerbation of these are an entirely different pathologic process from acute hæmorrhagic pancreatitis which demands immediate operation. The history in the hæmorrhagic type is a very sudden onset of upper abdominal pain that is not relieved by morphine, with a board-like abdomen and a moderately elevated temperature of 101° F. to 102° F., and a slightly elevated leucocyte count of from ten to twelve thousand and an extremely high polymorphonuclear count of around 95 per cent. These findings can

be compared with those found in the chronic disease and one should be able to make a differential diagnosis between the two.

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POST-OPERATIVE SHOCK FOLLOWING SPLENECTOMY FOR CHRONIC THROMBOCYTOPENIC PURPURA

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In this brief report I wish to draw attention to the rather frequent occurrence of post-operative shock following splenectomy for chronic thrombocytopenic purpura. I do not think that attention has hitherto been directed to the importance of this picture.

Before discussing the clinical picture I would like to present the histories of three personal cases of thrombocytopenic purpura which suffered from severe post-operative shock following splenectomy and which form the basis of this report.

Case I.—No. 262347. J. C., male, aged fifteen, admitted December 21, 1925, discharged February 11, 1926. Bleeding tendency first noticed about three years ago. For the past two years he has suffered from epistaxis. Following a tooth extraction he bled for twelve hours. No purpuric spots were noted on the skin. Hæmoglobin 83 per cent., red blood cells, 5,508,000, platelets 52,000; bleeding time three and one-half minutes, coagulation time five and one-half minutes. Tourniquet test negative within five minutes. No clot retraction within twenty-four hours. In the inside of the mouth and cheeks there are several petechiæ. Another rather large spot is noticed in the neighborhood of the tourniquet test. Four days after admission he bled profusely from the buccal mucous membrane and from his lips. There are many petechiæ now on the soft and hard palates. Hæmoglobin during time of observation had fallen from 83 per cent. to 68 per cent. *Diagnosis.*—Thrombocytopenic purpura.

Splenectomy was performed January 16, 1926, under general anæsthesia. A left upper quadrant oblique incision was made parallel to the costal margin. The spleen was found enlarged, adherent to the stomach but free on the parietal surface. The adhesions were divided. The gastro-lienal ligament was clamped and divided. The pedicle of the spleen was very short; it was divided between clamps, and the spleen was removed. A rubber tube was put into the subphrenic space. The abdomen was closed in layers. The patient returned to the ward in good condition. One-half hour later he suddenly went into deep collapse; the color was extremely pale, extremities and face were cold and clammy. Patient was extremely restless. A venous infusion of 500 cubic centimetres was given; this procedure was repeated three hours later. His condition improved during the evening and he recovered from the shock about eight hours after the operation. He made a good recovery and when seen recently was in perfect condition.

Case II.—No. 314225. B. M., female, aged thirty, admitted May 12, 1930, died May 15, 1930. History of having developed ecchymoses on the skin very easily for the last fifteen years. Severe symptoms had been present for only two years, consisting of large ecchymoses, severe epistaxis, intra-oral bleeding, metrorrhagia, and menorrhagia. This had been accompanied by headaches and nausea. Physical examination revealed the entire body to be covered by fine purpuric spots. In addition, there were several large ecchymotic areas. The spleen was palpable, but not markedly enlarged. A diagnosis of thrombocytopenic purpura hæmorrhagica was made and confirmed by blood findings. Red, white, and differential counts were normal, platelets

1,900, bleeding time twenty-five minutes, coagulation time fifteen minutes, the clot did not retract; tourniquet test was strongly positive.

Patient was transferred to the Surgical Service and splenectomy performed under general anæsthesia. The spleen was slightly enlarged. The lienophrenic ligament and a few adhesions had to be divided bluntly before it could be delivered. After ligation of the pedicle and after removal of the spleen, the operative field appeared dry. The abdomen was closed without drainage. About thirty minutes after the patient's return to the ward she went into profound shock. An intravenous infusion was given immediately, followed by a blood transfusion (500 cubic centimetres of citrated blood) about two hours later. Blood transfusion caused no great change for the better, and though an exploratory puncture in the right lower quadrant yielded no blood, it was thought that the possibility of bleeding was sufficiently great to justify exploration. The patient was taken back to the operating room. The wound was re-opened and a small amount of blood was found. The pedicle was dry, but blood had collected under the diaphragm, probably originating there from the division of the adhesions. Clots were evacuated and the subphrenic space was packed. The wound was closed again; one rubber tube being inserted. Another transfusion was given at once. Following this revision the general condition improved. Temperature mounted, however, and the patient was troubled by some abdominal distention and regurgitation of the stomach contents. To maintain fluids an intravenous infusion was ordered on the second day after the operation. During this she had a severe chill with rise of temperature to 106°, pulse became rapid and thready, patient cyanotic and bathed in sweat. Intravenous infusion was promptly discontinued. Death ensued a few hours later.

Blood count on the day of the exitus showed: platelets 375,000, bleeding time three minutes, leucocytes 15,600 with 90 per cent. polymorphonuclears.

Post-mortem examination showed a localized fibro-purulent peritonitis, moderate hæmorrhage into the peritoneal cavity, pulmonary œdema, ecchymosis of endocardium, bladder, and skin.

Epicrisis.—The re-laparotomy for suspected hæmorrhage was an error in judgment. Though a fair amount of fluid blood and clots were encountered, a free hæmorrhage was absent. The patient succumbed to localized infection.

Case III.—No. 321568. D. A., male, aged fourteen, admitted December 27, 1930, discharged February 15, 1931. History of bleeding gums, purpuric blotches, and repeated epistaxis for several years. On admission physical examination showed clotted blood in the nostrils, purpuric blotches, petechiæ, conjunctival hæmorrhages, palpable liver and spleen. Hæmoglobin 94 per cent., red blood cells 5,000,000, white blood cells 12,650 with 74 per cent. polymorphonuclears, platelets 40,000, bleeding time one hour and thirty-five minutes, clotting time two minutes, tourniquet test positive. He was transferred to the Surgical Service where just before operation his hæmoglobin was 82 per cent., bleeding time thirty-eight minutes, platelet count 80,000. Splenectomy was performed under general anæsthesia through an incision along the left costal margin.

The spleen was slightly enlarged without any adhesions. The patient left the operating room in excellent condition. Twenty minutes after he had reached the ward he suddenly went into a profound shock, became pulseless and ice cold, very restless and uncontrollable. An intravenous infusion was given immediately followed by 500 cubic centimetres of citrated blood taken from a donor, who was in the hospital during the operation and was kept in the reception ward to be available for immediate use, in case of sudden post-operative shock. Immediately following this transfusion, patient's pulse improved and condition became better during the evening. Air hunger, which had been observed before the transfusion, disappeared. The next morning his condition was excellent. About five days after operation he vomited a pus basin full of fresh blood. However, his pulse did not change very much and the circulation was very good.

Another transfusion was given following this hæmorrhage and the patient made a good recovery.

Two cases with a similar post-operative course of shock following splenectomy for chronic thrombocytopenic purpura are herewith given in abstract. They were operated by two of my colleagues at the hospital.

CASE IV.—No. 282556, 1927. Thirteen-year-old girl. Splenectomy in typical fashion. Upon return to her room the child was conscious, pulse good. Thirty minutes later the condition was very poor; the pulse was very weak. Two hours later the child went into shock; pulse could not be obtained. Though an immediate blood transfusion was ordered, the child died before arrival of the donor.

CASE V.—No. 294773, 1928. Patient was returned from operating room at 10.30 A.M. During the evening the pulse became very weak and irregular. She was put into shock position and received a Murphy infusion. The condition did not improve during the night. The next day pulse was still imperceptible at times, the body was cold and clammy. In the afternoon of the second day a blood transfusion was given. General condition improved immediately after the transfusion and the patient made an uneventful recovery.

In looking over the records of splenectomies performed at this hospital from 1926 to 1930 inclusive I was struck by the fact that whereas deep post-operative shock followed splenectomy for chronic thrombocytopenic purpura in five out of nineteen cases, a similar condition was not observed among seventeen splenectomies performed during this period for other causes.

The two deaths in this series probably could have been avoided, one case (II) if the proper diagnosis of shock instead of hæmorrhage had been made, the other case (IV) if an immediate transfusion had been given.

The sequel of events usually occurs in the following manner: the patient leaves the operating room in perfect condition. Respiration and circulation are normal. Either within an hour or a few hours after the operation the patient suddenly goes into deep collapse. The pulse is imperceptible, the skin is cold and clammy, the patient is very restless.

In the five cases reported above, the operations were of short duration and did not offer technical difficulties. The patients appeared to be good operative risks. While in this group of cases the post-operative shock usually occurs very soon after the end of the operation, delayed shock (six to twelve hours post-operative) may follow the splenectomy (Case V).

It is interesting to note that in Case V the post-operative shock lasted for twenty-four hours in spite of supportive measures. The serious clinical picture changed immediately after the blood transfusion.

Chronic thrombocytopenic purpura is at present the most frequent indication for splenectomy. For instance in this hospital more splenectomies were performed for this disease between 1926 and 1930 inclusive than for all other splenic diseases combined (19:17). As a rule post-operative and late results of splenectomy in this group of cases are excellent. For this reason it seems of some importance to point out the frequency of post-operative shock which may follow splenectomy for chronic thrombocytopenic purpura

(26 per cent. of our material). Properly timed blood transfusion may overcome this alarming emergency.

CONCLUSIONS

(1) For some unknown reason sudden post-operative shock seems to follow splenectomy for chronic thrombocytopenic purpura in a large percentage of cases. This observation is of practical importance, as shock and hæmorrhage are apt to give practically identical clinical pictures.

(2) Blood transfusion is the best method to combat post-operative shock following splenectomy.

(3) A properly tested donor ought to be present in the hospital at the time of operation for use in an emergency. The donor should be kept in the hospital for at least twelve hours, as late shock may follow.

THE ETIOLOGY OF INFLAMMATORY AND DEGENERATIVE DISEASES OF THE APPENDIX*

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Our knowledge of the etiology and prophylaxis of appendicitis is in the state it was in the later days of its clinical recognition by Reginald Fitz (1886), McBurney (1889), and Fowler (1894). At the present, our sentiment to appendicitis is much like that to the communicable diseases of childhood a few years ago. The sooner we have it the better off we are.

There are two diametrically opposed views in regard to the origin of appendicitis: (1) A circulatory disturbance of the appendiceal blood-vessels produces a necrosis or inflammation (Ricker,[1] Rosenow,[2] Portis[3]); and (2) the enterogenic theory which assumes that the disease arises from within the lumen of the appendix (Aschoff,[4] Heile,[5] Bowen,[6] Gross,[7] Niedermeyer[8]). All these authors, although adhering to the general conception, have different views of the mechanism that results in appendicitis. Aschoff believes that retention with a prolonged contact of the mucosa with pathogenic bacteria results in inflammation. Heile thinks that there is a trypsic action of an abnormal amount of fluid in the lumen of the appendix with a consequent necrosis of mucosa assisted by the appendiceal bacteria. Gross implicates inspissated fæcal material and Niedermeyer thinks that foreign bodies in the lumen are responsible for the lesion. The enterogenic school stimulated a number of analyses of the appendiceal bacterial flora (Isabolinsky,[9] Bagger and Mikkelsen,[10] and Warren[11]). These investigations demonstrated that the bacterial flora are varied, numerous, and that no single organism could be held responsible.

Another controversial topic is that of chronic appendicitis. Clinically, it is a more or less definite entity, but the pathologists are unable to agree to the criteria that constitute this condition. Among many theories of the etiology, Aschoff's[12] conception that chronic appendicitis is an end-result of an acute attack is probably the most widely accepted. Portis advances the interesting hypothesis of an interference with the blood supply due to adhesions and kinking. He does not believe that chronic appendicitis is an inflammatory condition.

Separation of the Retrogressive and the Degenerative from the Inflammatory Lesions of the Appendix.—In a survey of surgically removed appendices I found that 44 per cent. of them were free of an inflammatory lesion (exclusive of normal appendices). The patients' histories and their condition one year or more after the appendectomy demonstrated, however, that the appendix must have been involved. A study of the 44 per cent. of the

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appendices disclosed definite abnormalities. These abnormal changes consisted either of mucosal erosions or of an atrophy of the appendiceal wall. The pathological changes in greater detail had been described by me elsewhere.[13] It was evident that, though an inflammatory process did not exist, other types of abnormal structural alterations of the appendix may give rise to clinical manifestations. Since the introduction of the term appendicitis by Reginald Fitz, we have been constantly thinking of all conditions referrable to the appendix in terms of inflammation. The pathologist even stretches the definition of inflammation to accommodate changes in the appendix which he can not classify but which he appreciates to be abnormal.

Since the appendices could be separated into two groups (inflammatory and non-inflammatory) pathologically, a study of the patients' histories was made to determine whether a similar differentiation could be achieved clinically. It was found, that with a few exceptions, those histories could be likewise placed into two groups: One corresponded to the pathologically inflammatory class and the other to the retrogressive and the degenerative. The term appendicitis denotes inflammation and does not depict the retrogressive and the degenerative types of appendiceal lesions. The prognosis of the two groups vary. In order to convey this distinct difference between the two types of appendiceal disease I introduced[13] the term appendicosis for the retrogressive and the degenerative group. The clinical differentiation of the two groups is as follows:

Clinical Manifestations of

Appendicosis	*Appendicitis*
(1) Single attack, intermittent attacks or continuous discomfort.	(1) Attack well defined.
(2) Pain is dull and not severe.	(2) Pain colicky or sharp and moderate or severe in character at the beginning of the attack. It may continue or subside.
(1) Single attack, intermittent attacks or the right iliac fossa at the beginning or throughout the attack.	(3) Pain at first generalized and later localizes itself to the right iliac fossa.
(4) Nausea slight and frequently absent, vomiting rare.	(4) Nausea and very frequently vomiting.
(5) No rigidity or muscle spasm. Soreness on deep palpation over the right iliac fossa.	(5) Tenderness, hypersensitivity to touch, muscle spasm of varying degree over the right iliac fossa.
(6) No fever and no leucocytosis.	(6) Fever and leucocytosis of varying degree.
(7) In continuous type there is constipation, loss of appetite, general indisposition, lassitude, a frequent aching in the right iliac fossa and tenderness on deep pressure.	(7) Danger of perforation and peritonitis.
(8) No danger of perforation or any other complications.	

Etiology of Appendicitis and Appendicosis.—I observed that in a very large number of appendices either with inflammation or mucosal erosion type of appendicosis the initial lesion could be recognized to have appeared in the mucosa. Occasionally, particles of fæcal material were present in the mucosal furrows or "bays" and in some instances, firmer and sharper particles had pierced and injured the mucosa. (Fig. 1.) These observations were made possible by the study of stained longitudinal sections of the entire organ. A section so cut offered a view of the lumen and the opposing walls of the whole organ which could not be achieved by the usually prepared cross-sections.

A röntgenological study of the appendices of normal persons was made. It was noticed that the appendix filled passively but expelled material by

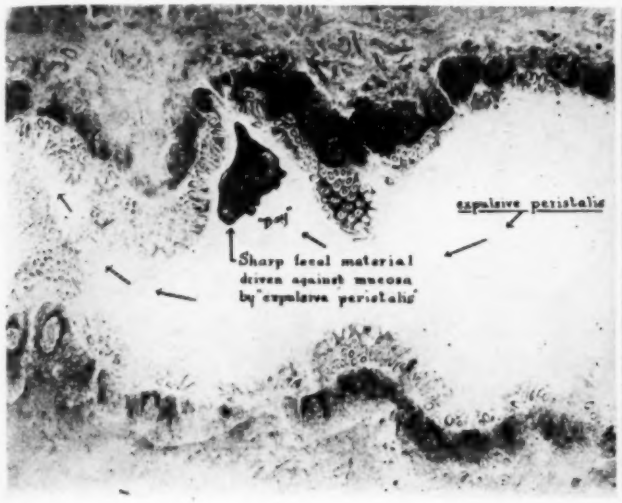

FIG. 1.

FIG. 2.

FIG. 1.—Longitudinal section of part of appendix shows a sharp fæcal body with a mucosal injury opposite. The arrows indicate the direction of peristalsis.

FIG. 2.—The appendix is seen expelling material—expulsive peristalsis. The tip is still visualized; the rest of the tract is free of barium.

peristaltic contractions which began at the tip. (Fig. 2.) These peristaltic waves continued for hours until the entire organ was free of barium. Jordan[14] had made similar observations. In view of these findings it was concluded that during the process of expulsive peristalsis sharp particles of fæces are driven into the mucosal bays and due to repeated impacts they pierce and lacerate the appendiceal mucosa. These findings and conclusions do not, however, explain the conditions which determine the causation of appendicitis and appendicosis.

To determine the relation of the bacteria in the appendiceal lumen to the production of lesions, a bacteriological study of normal appendices, those with appendicitis and with appendicosis, was made. Similar to the results obtained by most of the other investigators, no particular organism or group of organisms was found to be common to one or the other type of appendiceal

lesion, nor did these bacteria differ from those in the normal appendices. Smears of the appendiceal contents and of the mucosa from all parts of the appendix controlled the complete isolation of all the bacteria present in the organ.

Although numerous investigators determined the type and number of the appendiceal bacteria, no determinations of the pathogenicity of the isolated bacteria were done. If the bacteria have any etiological relationship to the mucosal injuries, injection of these bacteria into similar tissue may elicit their pathogenicity for this particular type of tissue. Consequently, a culture of each isolated microorganism was injected intracutaneously into dogs. It was found that all or some of the bacteria from appendices with appendicitis produced abscesses in the areas injected. (Fig. 3.) On the other hand, the bacteria obtained from the mucosal erosion type of appendicosis seldom

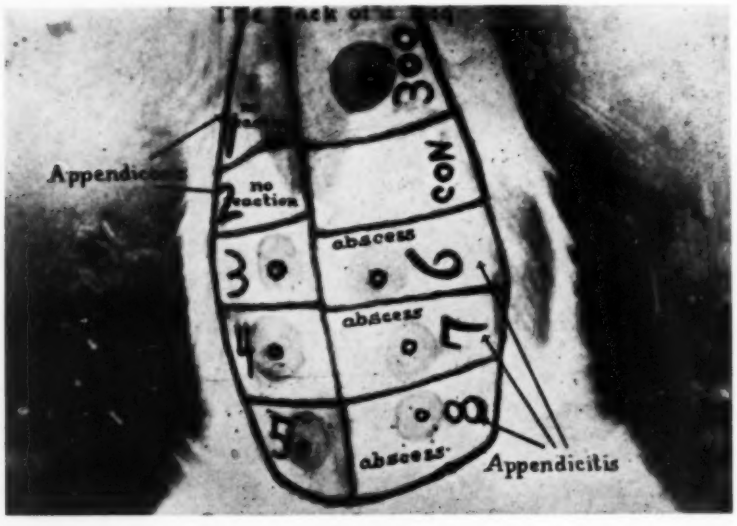

FIG. 3.—Reactions from intracutaneous injections of appendiceal bacterial cultures.

showed a reaction or only a slight induration in the skin of the animal. It was deduced that though the bacteria may be similar in type their pathogenicity varies and determines the formation of an inflammatory or a degenerative lesion. In presence of pathogenic organisms the mucosal injury produced by sharp fæcal particles driven by the expulsive peristalsis results in a mucosal ulcer which is followed by various degrees of inflammation (appendicitis). If the organisms are not pathogenic, no inflammation sets in and a mucosal erosion results. Since the type of the microorganism is the same in appendicitis as in appendicosis, it is assumed that the difference in the pathogenicity is due to factors resident in the lumen of the appendix. These factors remain subjects for further investigations which may eventually lead to artificial methods in rendering the appendiceal bacteria non-pathogenic.

The retrogressive type of appendicosis which I designated[13] "pressure atrophy type" is produced by a different mechanism. The change in this type

is that of compression of the wall. From the röntgenological observations it is concluded that this condition is due to stagnation in the colon. There is interference with emptying of the appendix and the continuous pressure increases the appendiceal contents, which distend the lumen and lead eventually to atrophy of the wall. The outstanding and frequent symptom in this type of appendicosis is constipation accompanied by lassitude and an indefinite complaint of indigestion.

Summary.—Retrogressive and degenerative lesions of the appendix (appendicosis) are differentiated clinically from the inflammatory lesions (appendicitis).

The mechanism of production of appendicitis and appendicosis is explained. Sharp particles of fæcal material are propelled by the expulsive peristalsis of the appendix into mucosal bays and injure the mucosa. In presence of an environment within the appendix favorable for growth of bacteria appendicitis results; in absence of such an environment the bacteria are rendered non-pathogenic and appendicosis is the outcome.

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MYXOGLOBULOSIS (VON HANSEMAN) OF THE APPENDIX

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Appendectomy has become a major part of everyday surgery. The majority of cases present such an ordinary pathological picture that the surgeon usually approaches the operation with no real apprehension as to clinical findings. However, though it is rarely encountered, we do find mucocele and pseudomyxoma of the appendix. Because of the comparative scarcity of literature on the subject, this paper is presented.

Obliteration of the appendicular lumen due to foreign body, *i.e.*, fecalith, with mucous degeneration of the distal portion, was first described by Rokitansky in 1861. Virchow next mentions, in 1863, retention cysts of the appendix which resemble mucous glands. In 1901, Frænkel reported an autopsy finding where large gelatinous masses, originating from the appendix, were found in the cæcal fossa. As recently as 1909, Elbe reported that only 150 cases of this unusual disease were to be found in the literature and the statistics of Glawirovsky show that of all appendices operated and reported upon, only 0.6 per cent. show this anomaly. Even more unusual is the condition first described by Von Hanseman. He reported that upon examination of a cyst in the appendix, he found, situated near mucous masses, small kernels resembling sago seeds or fish roe. This he termed myxoglobulosis.

If, in the healing process of an appendicitis, stricture forms, sterile mucus retention might result distal to this obstruction. This is called mucocele. This stricture is usually caused by inflammation. However, various agents such as tuberculosis, dysentery, carcinoid tumors, as well as small echinococcus cysts near the cæcal end of the appendix can be considered factors in causing obliteration. Robbed of the possibility of draining into the cæcum, the mucus becomes thicker and gelatinous, the mucin changing into pseudomucin and colloid and forming a homogeneous mass. The mucous membrane of the appendix is either destroyed through pressure or forms small diverticula. Von Hanseman found these diverticula to be usually situated opposite the mesenterial attachment. In them or in the excretory canals of the mucous glands, broken-up cells will accumulate from which the central portions of the previously mentioned kernels are formed. Lymphocytes and stellate cells are found in them very rarely. The kernels present on cut surface an opaque centre and glassy outer cover. Their size varies from a few millimetres to one centimetre.

In his report, Michaelson[6] presents his findings of a gelatinous mass with a network of connective tissue-forming strands and occasional epithelial cells of cylinder and columnar type. Based on findings of his own and of Nael-

sund, who produced this condition experimentally in animals, Michaelson contends that the appendicial epithelia may be implanted in the abdomen and may proliferate. This may be compared to the proliferation of normal epithelium in the traumatic epithelial cysts in the so-called atticus fistulæ or with the retention cysts in the outer chamber of the eye. Connection of the cyst with the free abdominal cavity through perforation will cause the formation of gelatinous deposits in distant parts and gives the picture of pseudomyxoma peritonei.

Two aspects of the disease present themselves in the clinical picture. The first is circumscript and is caused by the fact that the pseudomucinous fluid remains confined within the walls of the appendix, thereby forming a cyst. The second is diffuse and is caused by the fluid diffusing between the layers of the cæcum, thereby producing myxomatous degeneration. Owing to the thin wall of the cyst, traumatic or spontaneous rupture may occur. In the case of Frænkel, reported in 1910, disseminated pseudomucinous peritonitis was present as a consequence of a ruptured cystic appendix.

If spontaneous perforation takes place, the gelatinous fluid will seep through the small opening and by means of peristalsis of the intestines will be deposited even in distant parts of the abdomen. It is a moot question how the gelatinous material thus distributed proliferates. In Ewing's[7] opinion, the pseudomucinous material passes into the lymph spaces of the peritoneum. To quote the opinions of Werth, Gunzberger and Westphalen: "These spaces become distended and ruptured, the material infiltrates the meshes of the peritoneum, round-cell infiltration, growth of granulation tissue and proliferation of endothelium result and the peritoneum is everywhere thickened by a painless form of peritonitis." It seems most probable that the appendicial mucous cells carried away in the peritoneal cavity continue to function and to produce pseudomucinous fluid. Otherwise, how can the occasional presence of enormous amounts of gelatinous material be explained?

Ewing further quotes Wirth and Polano, who give another possibility, namely, that mucous fluid without tumor cells may migrate in the lymph channels along the portal system into the liver or into the appendix and there set up new growths. Although lymphatic connection between the right ovary and the appendix is not yet firmly established, still our finding of an enormous pseudomucinous cyst of the right ovary associated with the simultaneous finding of myxoglobulosis of the appendix as in our case reported below, further substantiates this belief.

Present-day knowledge is not sufficient to answer the question as to whether the pseudomucinous fluid in the abdominal cavity is inflammatory or neoplastic. That it may be inflammatory is borne out by the fact that a pseudomucinous condition has been reported in some cases to have spontaneously regressed while in others it took a neoplastic course.

Clinically, myxoglobulosis gives the picture of chronic appendicitis. The appendicular symptoms are due to pressure changes of the enclosed gela-

tinous masses. The symptoms are analogous to those described by Ashoff in stone-free dyskinetic cholecystic attacks which are of a nervous reflex nature. *Per se* it has never been diagnosed. Usually it is an occasional finding or is diagnosed only at autopsy, as in the cases of Von Hanseman and Michaelson. The obstruction in the appendix is usually the result of an appendicitis or tumors, as in the cases of Spassokukoczky where a carcinoid, and that of Huter, where an adenocarcinoma was found. While pseudomyxoma peritonei is found mostly in women, myxoglobulosis shows prevalence in males. In Birkenfeld's[1] statistics of twenty-six cases, only five women were affected by the disease.

Therapy consists of the removal of the diseased apendix. In pseudomyxoma peritonei, as much as possible of the gelatinous material should be removed. If the disease is of ovarian origin, the affected ovary and con-

FIG. 1.—Shows the size of the appendical cyst. Mesenterial fat attached. No constricting band separates the more and less distended parts.

sidering the bilateral tendency of the disease, it might be advisable to remove the other ovary and the omentum. Bearing in mind that a malignant degeneration may take place, post-operative radiation is justified.

CASE HISTORY.—A woman, fifty-two years of age, by occupation a housekeeper, first seen August 21, 1931. For the last five months observed fullness in the abdomen with stubborn constipation. Lately abdomen has grown larger but has not caused her any other symptoms except discomfort and short breath on exertion. Menses were regular since eleven years of age, lasting four to five days, without pain or discomfort. Three births; no abortions. At forty-three had a severe hæmorrhage, following a menstrual period and lasting fourteen days. After curettage her periods became normal again and continued so for three months, when again metrorrhagia developed and continued for three months without cessation. Examination revealed the presence of fibroid tumors of the uterus with bilateral ovarian cyst. Complete hysterectomy and partial oöphorectomy were done ten years ago. She never had any attacks attributable to appendicitis. She has been well ever since until recent illness.

Examination revealed a large fluctuating mass, the upper end of which reached the xyphoid process. No free fluid in the abdomen. No tenderness on pressure present. Appendix region not tender. No resistance was palpable inasmuch as the cystic tumor filled the abdominal cavity.

At operation September 8, 1931, a large ovarian cyst was found emerging from the stump of the right ovary. The left ovary had been entirely removed at the previous operation. Aspiration of the ovarian cyst was done, whereby six quarts of pseudomucinous, sanguinolent fluid were withdrawn. The cyst and ovarian rest were removed.

As a routine procedure the appendix was looked for and found to be distended to form a smaller cyst measuring three by two inches. The cyst wall was transparent with a few lime deposits inclosing an apparently clear fluid. No constricting band was seen and the pear-shaped cyst seems to continue without break to the also distended proximal portion of the appendix. (FIG. 1.) The appendix was removed.

Histological examination showed the fluid withdrawn from the ovarian cyst to be pseudomucin. The wall did not show anything unusual.

Section of the proximal end of the appendix showed hypertrophy of the muscle coats with polymorphonuclear infiltration of the mucosa and submucosa. Occasional eosinophile and stellate cells present. Normal gland structure partly destroyed. The cystic part contains thickened mucus and an abundance of small globules, their sizes ranging from millet to sago seeds. A few loose fibrous bands traverse the cystic cavity. Cut surface of the kernels is grayish and around the opaque centre a slimy outer cover is seen. The centre of these globules consists of colloid and broken-up cells, which could not be identified.

Patient made an uneventful recovery. When seen twice since then the scar remains firm. She is apparently in good health, without any sign of recurrence.

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BRIEF COMMUNICATIONS

INFLAMMATORY CYST OF THE BREAST

CHRONIC cystic mastitis, blue-domed cyst and serous-retention cysts are considered fairly common conditions, but it is quite rare to see the development of a solitary cyst following a chronic abscess However, chronic abscesses are occasionally found, especially those being due to specific diseases, particularly tuberculosis. Reclus[1, 2] recorded a case in which a small nodule appeared with a mastitis after delivery and which suppurated six years later.

Abscesses of the breast are occasionally seen as a complication of pregnancy. Spontaneous rupture of the abscess is unusual, due to the deep situation of the abscess and the pain experienced by the patient, which nearly always forces them to consult a physician. Chronic pyogenic abscesses are unusual, thereby probably accounting for the absence of a reported case similar to this one.

CASE I.—A colored woman, aged thirty-two years, was admitted to the Emory University Division of the Grady Hospital August 31, 1931. The chief complaint was an enlargement of the right breast. This came on during a pregnancy six years before. The mass was described as being small at the onset and accompanied by considerable pain. The swelling increased for several days and then finally ruptured spontaneously. A thick yellow pus discharged for four or five days and then the opening closed. The baby was delivered a few months later. However, she was unable to nurse it from the right breast due to pain. At no time did the breast return to its normal size.

One year later the woman became pregnant and the breast again began to swell and was very tender. A spontaneous rupture with discharge of a large amount of pus occurred a short time afterwards at the site of the original opening. Closure of the opening took place in a few days. There was a period of quiescence of four years until a few weeks before admission, when the swelling increased but was not accompanied by pain as at former times. The discharge from the opening then was a thick, brownish, watery fluid.

Physical examination was non-essential except for the right breast. There was a globular swelling of the entire breast, which measured 6.5 by 6 centimetres. A small stellate, depressed scar was located three centimetres to the right of the nipple. The mass seemed to occupy the entire breast, which was soft and semi-fluctuant. There was no enlargement of the axillary nodes.

Laboratory examinations, including blood Wassermann, were negative.

A probable diagnosis of cyst of the breast was made and operation performed August 15, 1931. An elliptical-shaped incision was made around the entire breast and it was removed down to the pectoral muscles. (Fig. 1.) On opening the breast there was revealed a thick-walled sac which occupied the entire breast, being surrounded by only a small amount of subcuticular tissue and fat. The cyst measured six by five centimetres. The sac contained a thin, odorless, straw-colored fluid. Two definite layers of the wall of the cyst were made out. The outer was a light-colored, thick, fibrous one and measured two millimetres in thickness. The inner one was irregular, dark and brown, with a thickness of three millimetres. At the upper and outer portion of the cyst was a small tract which lead to the scar on the skin surface. (Fig. 2.)

Microscopical examination (Dr. E. L. Bishop) showed a fibrous capsule outside of which was an area of acellular connective tissue with several groups of acini and some

FIG. 1.

FIG. 2.

FIG. 1.—Outer surface of breast showing opening on the skin.
FIG. 2.—The opened cyst showing two layers of cyst wall with the cavity and tract leading to the surface.

normal-appearing fatty tissue with scattered lymphocytes. (Fig. 3.) There was a clear-cut line of demarcation at the cyst wall, which was densely fibrous, with scattered small

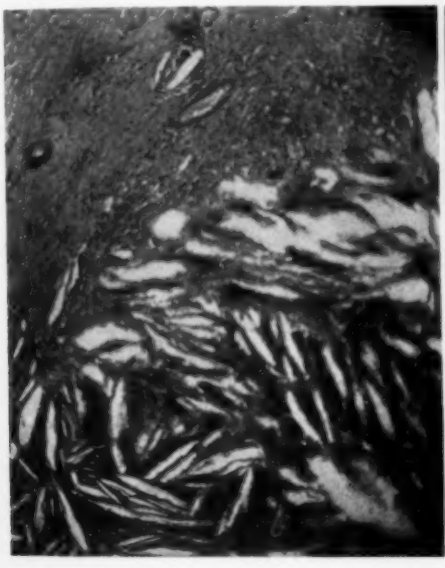

FIG. 3.

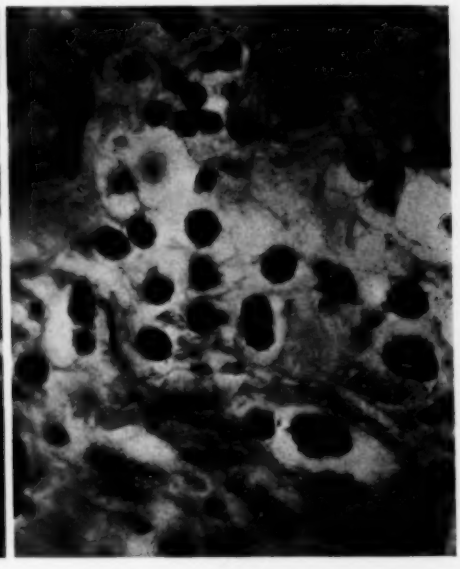

FIG. 4.

FIG. 3.—Lower-power microscopical picture showing the two layers of wall.
FIG. 4.—High-power magnifications showing large, premature fat-cells and the spaces left by cholesterin crystals.

injected vessels. There were no cellular areas in the capsule. Lymphocytes and vessels were present in increasing numbers as the central portion was approached. At the

line of the cyst cavity was a thick area of vascular granulation tissue and a large number of lymphocytes, plasm-cells and a few leucocytes. In several of the larger vessels there were numerous leucocytes. Few areas of fat-cells, some proliferating, and many degenerating, were seen. (Fig. 4.) A great many elongated crystals were represented by open spaces with a tendency for foreign-body giant cells to form about these crystals. There were scattered areas of necrosis and small areas of hæmorrhage with some blood pigment in a few areas. No glandular structures of anything of neoplastic character was seen.

Diagnosis.—Chronic abscess with suggestive traumatic fat necrosis.

This case exhibits considerable resemblance to traumatic fat necrosis, but at no period was there a history of injury. However, according to Gattleman and Zemansky,[3] it is questionable the part trauma really plays, as in their twenty reported cases it was an infrequent finding.

If this case had been seen at an earlier date before the serous effusion accumulated, the picture might have been similar to a fat necrosis, which clinically must always be differentiated from carcinoma. The probable sequence of events in this case was abscess formation on two occasions with spontaneous drainage and rapid closure of the opening, leaving a pyogenic wall which did not heal from within outward and which assumed secretory characteristics.

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MENINGEAL HÆMORRHAGE WITHOUT INTRACRANIAL SYMPTOMS

IT IS usually on the symptoms and signs that a diagnosis of meningeal hæmorrhage is made. A case of unconsciousness with the primary concussion followed at a later period with consciousness which again gives way to a second unconscious period carries great weight in diagnosing meningeal hæmorrhage. There may be any form of scalp, skull or brain injury with the rupture of the meningeal artery. Hæmorrhage requires trephining and ligation of the bleeding point. If depression occurs it requires trephining and elevation. If a simple fracture of the vault occurs without hæmorrhage, depression or brain symptoms, or if a slight depression occurs without brain symptoms or if symptoms were present and are abating, it can be treated expectantly.

If the depression is marked a trephine should be done even if no symptoms are present, except in young children with pliable skulls. DaCosta advocates trephining all cases of fractures of the base; first it is exploratory

and again it is a preventive trephining against later complications, as epilepsy, insanity, change of character and septic inflammations, *etc.*

CASE REPORT.—M. J. N., a four-year-old child, was brought to the Guam Naval Hospital with hematoma of scalp and history of injury. Three days before admission when he was crawling out from under a house being constructed a piece of lumber four by four inches square and about three feet long fell from the roof and with one end struck him on the right side of the head. He was knocked unconscious immediately; a swelling developed on the right front temporal and parietal areas. He was a well-nourished child; the right side of his head and eye were swollen. No open wounds were seen.

There was a large hematoma on the right frontal temporal and parietal regions. The right eye was nearly swollen shut. There was no subconjunctival hæmorrhage although he had a black eye. There were no ocular muscle palsies, the pupils reacted normally and were equal and regular, and the fundi showed no abnormalities. There was no facial palsy or weakness, the tongue was not paralyzed, there was no nasal, pharyngeal or other bleeding. No spinal fluid to indicate fracture into the nasal cavities. The ears showed no hæmorrhage or spinal fluid. Battles' sign not present. There were no external open wounds anywhere on head. No fracture or depression could be felt. The hematoma had its hard "rim" around it. The neck was normal. The chest and abdomen were normal.

The reflexes of the extremities were normal. Sensation was normal. No difficulties with urination or defecation.

Spinal fluid.—No blood, normal cell count and globulin but the pressure was increased a little on admission.

X-ray showed the skull fractured throughout nearly three-fourths of the circumference of the vault and extending into the base!

Comment.—We have here a case of skull injury caused by a direct force of the bursting type. A hematoma formed but no spinal fluid was under the scalp. He was not seen at the hospital for over seventy-two hours after his accident and his history suggested merely a concussion at the time of the accident which lasted about two hours. After the reaction from this he had no further unconsciousness at any time. On admission he had no palsy, no headache, no vomiting, no choked disc, no face flushing, no altered pupils, no abnormalities of blood-pressure, pulse or circulation, no eye-muscle palsies, no subconjunctival, nose or ear hæmorrhage, no stupor or excitement, no altered function of urination or defecation and only a slight rise of temperature, yet he had a fracture of his skull which extended nearly three-quarters of the way around the skull and extended into the base. He was symptomless in spite of an extensive injury. No external wound was present except the hematoma which showed that a contusion had been suffered. The only suggestion of intracranial injury was the increased pressure of the spinal fluid and this was only suggestive as the child was wiggling and jumping while the tap was being made. His pulse was not irregular at any time after admission. The question of treatment was to be decided upon.

As a large hematoma is a possible source of embolism and as the fracture seemed to extend into the base it was decided to open the hematoma, explore the skull and possibly trephine. The X-ray suggested an area of depression which gave one more stimulus to operate. Operation was done

under ether and with rigid asepsis as we had an old bloodclot to deal with. Upon opening the scalp the extensive fracture was found and in the temporal region an area about the size of a quarter was found markedly depressed. A trephine opening was then made just above this area and it was elevated. The fracture line was rather wide and considerably separated. After the trephine opening had been made a clot was found on the dura about the size of a half-dollar, which, when removed, exposed two small tears in the middle meningeal artery. At a short distance from this area another clot was found which seemed to be from bleeding from the fracture line itself. All clots were removed, bleeding stopped by ligatures and bone wax and the wound closed. There was no subdural bleeding. He was kept in bed one month, he had a good and speedy convalescence, and left the hospital in good condition. He was given urotropin before and after operation.

This case may have got well if we had done nothing but possibilities of embolism from the hematoma, and of late effects from the injury and the clots such as epilepsy, insanity, infections or change of character, *etc.*, must not be lost sight of. He had no symptoms and yet he had a very extensive fracture with extradural hæmorrhage. It is possible that the skull fracture, being so extensive, allowed the top to give and thereby no intracranial pressure was caused. The relief of the pressure was accomplished by a fracture—separation substitute for trephining; that is, prior to operation.

Now, six months after the injury, there are no after effects such as palsies, hernia cerebri, insanity, epilepsy, change of character or inflammatory phenomena.

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A DOUBLE-BREASTED MATTRESS SUTURE

In no field of surgery is there more of a demand for an exact technical procedure than in the repair of large ventral hernias. These hernias are either primary, such as an umbilical hernia, or secondary to some abdominal operation in which suppuration of the abdominal wall, including the fascia, occurred. These hernias vary in size; some of their hernial openings are large enough to admit a hand. The details of the removal of the sac and the separation of adhesions are familiar. The closure of the hernial opening as described in most text-books is accomplished by overlapping the upper flap over the lower flap in a transverse direction, with interrupted chromic sutures.

The suture that the writer is about to describe has all the advantages of the mattress suture, but, in addition, it not only brings together the free

edge of the lower flap to the under surface of the upper flap, but it also brings together the free edge of the upper flap to the anterior surface of the lower flap, thereby obtaining a double line of approximation with a smooth inner peritoneal and outer fascial surface.

Fig. 1 enables one to visualize the various steps of this new suture. A No. 2 or No. 3 double chromic suture on a good, strong, curved needle is used. The suture enters at 1 in the upper flap about an inch away from its free edge; passes through the free edge of the lower flap, down to its peritoneal surface. It then passes about a quarter of an inch across to the left through the free edge of the lower flap, back again through the upper flap, again an inch away from the free edge. The suture then passes down to

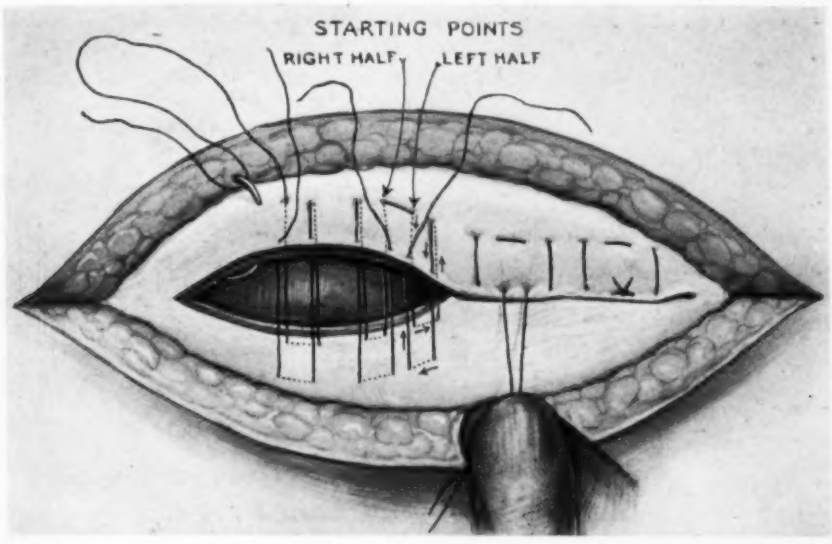

FIG. 1.—A double-breasted mattress suture. From left to right as it applies to patient. The first suture is completed. The ends of the second suture are pulled upon, approximating the flaps preparatory to tying it. The third suture indicates its complete course taken through the flaps. Note the pulley effect at five points of the suture. The arrows indicate the course of the left half; the same course is taken by the right half but in the opposite direction. To the extreme right only half of the suture is completed. The suture may be continued to complete its other half (as indicated by the needle) or the ends of the one-half may be tied and accomplish the same result but only for half the distance. This is especially applicable when only a remaining small gap in the fascia is to be approximated. This illustration applies to a hernia closed in a transverse direction. To visualize a hernia closed in a longitudinal direction, all one has to do is to hold the illustration in a vertical position.

the free edge of the upper flap and through the lower flap to its peritoneal surface, which is about an inch away from its free edge. The needle then passes from the peritoneal surface back to the right a quarter of an inch and passes through from the peritoneum through the lower flap and through the free edge of the upper flap reaching the outer surface of the fascia. This needle is then unthreaded, the other end of the same suture, which is left long, is threaded on the needle and passed through the upper flap and the free edge of the lower flap about a quarter of an inch to the right, and from then on the same steps are repeated until the needle reaches to the

free edge of the upper flap a quarter of an inch away from the other end of the suture. (Fig. 2.)

When these two ends are pulled upon the upper flap overlaps and becomes approximated to the lower flap in the same manner as do the flaps on a double-breasted suit. The peritoneal surface feels smooth, with no wrinkling; the outer aspect appears evenly approximated, with no dead space. Three or four such sutures accomplish a perfect closure of even a large ventral hernia. One of these sutures is sufficient to close the average epigastric or umbilical hernia. Should the incision of the hernia be vertical

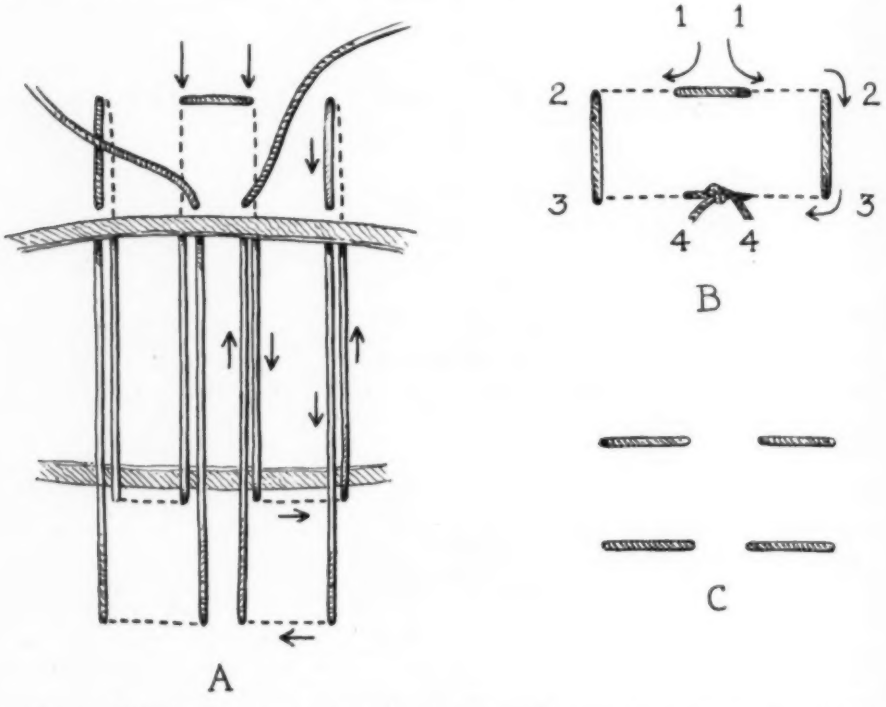

FIG. 2.—Diagrammatic.—A.—Presents the suture passed, but not tied. The direction of the two halves is indicated by the two arrows on top. Follow the course of the left half as indicated by the arrows. The right half takes the same course but in the opposite direction. B.—Shows the suture tied as viewed from its outer aspect. 1 and 1 indicate the start of the respective halves of the suture. 1-4 indicate the points where the suture passes through both flaps. The dark lines indicate the loops of the suture on the outer aponeurotic surface. The dotted lines indicate the loops on the inner peritoneal surface. C.—Indicates a view of the suture as would be seen from within the abdominal cavity.

the same procedure can be used by overlapping the flaps in a longitudinal direction.

An attempt to close the hernial opening with this suture impresses one with the ease with which these flaps automatically approximate. This is accounted for by the pulley-like effect produced when the free ends of the suture are pulled upon before they are tied.

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THIOCRESOL IN WOUND HEALING AND IN SKIN GRAFTING

REIMANN,[1] in 1930, published an original article on the clinical use of thiocresol for the stimulation of wound healing, reporting excellent results. With the exception of a second paper by Reimann,[2] in 1931, dealing with the further use of thiocresol to excite cell proliferation and thickening of the skin, there have been no other reports commenting on the clinical value of this drug.

In his first publication, Reimann based his theory on the results of Hammett,[3] who found that the essential difference between the nucleus of a cell in mitosis and the nucleus of a cell in the resting state was the "rearrangement of the sulphur in the molecules, so that this element appears in a chemical group, Sulphydry;[1] *i.e.*, SH-". Applying this discovery clinically, he deduced that sulphur in the proper form would stimulate wound healing. This he and Hammett[4] demonstrated on rats. Unfortunately, the SH- group also stimulated bacterial growth. Therefore, Reimann attached cresol to the SH- radicle, forming a labile compound, thiocresol. Applied to wounds, the cresol splits off, inhibiting bacterial growth without retarding the cellular progress. Bettmann[5] described a similar problem which he met by the incorporation of oxyquinoline sulphate and chlorbutanol (antiseptics) with scarlet R ointment (stimulating to the epithelium).

We have used thiocresol since the publication of Reimann's original article. We have applied it impartially on denuded areas resulting from burns, on sloughs (traumatic or surgical), decubitus ulcers, and on all other areas where denudation has been present. We are convinced that Reimann's treatment has benefited denuded areas which had been resistant to all other methods of treatment, that a tough and durable epithelium is produced, that convalescence is shortened, and that the method has the added advantage of simplicity and economy. As examples of our results the following cases are reported:

CASE I.—A male, aged fifty-five years, was admitted June 27, 1931, with second- and third-degree burns of both feet and ankles. While asleep in a park, a boy had poured gasoline on his shoes and set them on fire. His admission temperature was 102° F., pulse was 128, and respiration 30. Tannic-acid treatment was started immediately, spraying 10 per cent. tannic acid every fifteen minutes. A black crust formed, but the patient's temperature remained high. Therefore, on July 2 the crusts were removed and extensive suppuration was found underneath. Saline and magnesium sulphate compresses were applied continuously until July 8, when treatment with thiocresol was started. At the end of forty-eight hours a definite increase of epithelium was noted, especially on the left foot. July 15 the left foot was entirely healed; and on the 21st the right foot and ankle were also entirely healed. The reason ascribed for the slower healing of the right foot was that there had been a greater loss of the deep tissues.

CASE II.—A male, aged sixty-three years, was admitted June 29, 1931, with the diagnosis of second-degree burns of right foot and ankle, also received from gasoline burns, received under the same circumstances as Case I. On admission, the temperature, pulse, and respiration were normal. Tannic-acid treatments were started, and again the result was suppuration underneath the black, dry crusts. Continuous saline and boric compresses were applied from July 1 to the 9th, when thiocresol was started. Healing was complete on July 18. He was discharged August 5, 1931.

The method used in the application of thiocresol moistenings was that described by Reimann. A 1-10,000 solution of thiocresol is poured on pieces of gauze which are applied directly to the wound. Over the moist gauze

should be wrapped a sheet of rubber or oiled paper to prevent too rapid evaporation. The frequency of moistening the gauze depends on the size of the wound, the place of the wound, the amount of healing present, and the amount of evaporation that has taken place. As a rule, it is necessary to apply fresh solution every four hours. As pointed out by Reimann, fresh solutions should be used. There are two ways of preparing a fresh solution of the required strength; either the method originally described which is as follows: 1-100th gram of the crystals dissolved in 5 cubic centimetres of 95 per cent. alcohol, diluted in 100 cubic centimetres of distilled water, giving a 1-10,000 solution; or a stock solution may be made up of the crystals dissolved in alcohol and diluted with water as the occasion arises.

We have not noted the too extensive granulations supposedly formed through the prolonged use of thiocresol. It has been used continuously for as long as three weeks and longer without this reaction taking place. Therefore, the admonition of using the solution for forty-eight hours and the discontinuing it for twenty-four hours seems unnecessary. We have observed a continuous and rapid proliferation of epithelium from the wound margin and from dormant central islands with a continuous improvement in the whole wound appearance. The epithelium grows whether suppuration is present or not. Neither have we noticed the blister formation described by Reimann in his second paper.

Since the beneficial action of thiocresol is due to the stimulation of mitosis, the early successes prompted a trial of the treatment as a post-operative dressing on skin grafts. Results on two cases follow:

Case III (Fig. 1).—A man, aged twenty-three years, was admitted July 8, 1931, suffering from second- and third-degree burns of both legs. On admission the temperature, pulse, and respiration were normal. Tannic-acid treatment was started. But, on July 13, the temperature went up to 102°, pulse to 100, while the respiration remained normal. On July 16, the tannic-acid crusts were removed, and from then on the temperature which had remained almost constantly at 102° slowly decreased so that by the 22nd it reached normal. But the condition of both of his legs was not at all what could be desired. Moist dressings of saline and boric solutions were applied continuously. In a week the temperature again began to rise, so that on August 4 it reached 103°, and from then on it showed a septic curve, reaching at times 104° in the afternoon and dropping to normal in the morning. The condition of his legs became steadily worse. All the surface of both legs from below the ankles to above the knees were completely covered with soggy granulations overlaid with a thick layer of purulent exudate. In places loss of the deeper tissues took place, so that craters one inch in depth could be found. The pain was intense so that the dressings became more and more difficult. Contractures were beginning, the knees flexed and feet drawn down by the Achilles' tendons. The patient finally became unmanageable. In such a condition he was referred to our service September 4, 1931. The next day Thiersch grafts from the thigh were placed on both legs. All the granulating surfaces could not be covered, nor was such an attempt made. To the grafted areas were applied continuous moist dressings of 1-10,000 thiocresol. The dressings were not removed until ten days post-operatively. Underneath the purulent discharge were found islands of grafts which covered most of the previously denuded areas. The thiocresol dressings were continued with the hope that no more grafts would be necessary. The dressings were not changed

for periods of eight to ten days. At the end of twenty-eight days the result was perfect, the denuded areas being covered with healthy epithelium except at the places where there had been a greater loss of the deeper tissue. Over these areas were applied more Thiersch grafts. By October 24 all the previously raw areas were covered with epithelium (Fig. 1) and the patient was up on crutches. Two weeks later he was walking unaided, and in another two weeks he was driving a car.

Case IV.—A male, aged twenty-six years, was admitted November 18, 1931, with a terminal denudation of an amputation stump of the upper third of the left humerus. The area measured four by three inches. Thiersch grafts taken from the thigh were

Fig. 1.—Lateral view of Case III, showing the final result of the extensive burns following the use of Thiersch grafts and post-operative dressings with thiocresol.

placed on the wound. The post-operative treatment consisted of continuous moistenings with thiocresol. Two weeks later he was discharged to the Out-patient Department with almost complete epithelization. Two days later all dressings were removed, the denuded areas being completely covered with durable epithelium.

Comment.—Thiocresol has proven to be very stimulating to wound healing and of real clinical merit. In none of the cases have we found the granulations growing as fast as the epithelium, thus simplifying the technic. It has not been necessary to do anything but apply the solution to the gauze bandages wrapped about the lesions and leave them undisturbed. We have

observed that after the removal of the wet dressings healing seems to progress almost as rapidly as under the thiocresol compresses, indicating a cumulative action on the epithelial cells. This might prove of value in the use of thiocresol moistenings on ambulatory cases.

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NOTE ON THE ETIOLOGY OF ACUTE PANCREATITIS

We report the end-result of a gastroenterostomy for pyloric stenosis due to carcinoma that not only blocked the pylorus completely, but also, after a time, the gastroenterostomy opening, resulting in an apparently complete exclusion of the duodenum, the biliary system and the pancreas, which led before death to huge dilatation of the duodenum, forcing of the sphincter of Oddi, a wide-open pancreatic duct and a common duct big enough to admit the average thumb with dilatation of all the branches of the hepatic ducts far up into the liver. The case is especially interesting because of its bearing on the etiology of acute pancreatitis. A brief résumé of the case is as follows:

A man, aged sixty-seven years, was admitted to hospital with a history strongly suggestive of carcinoma of the stomach. Röntgenograms showed a lesion of very long standing with a hugely dilated stomach. When his abdomen was opened there was found only a hard, fibrotic, somewhat puckered plaque about the size of a fifty-cent piece on the anterior wall of the stomach just at the pylorus, apparently an old ulcer, with almost complete obstruction of the pylorus. The gall-bladder contained a few faceted stones but was very little thickened. No gross evidence of carcinoma was recognized and a posterior gastroenterostomy some six inches from the pylorus was done and a tube put in the gall-bladder after removing the stones. The common duct was not dilated and no stones were felt in it. He left the hospital in six weeks, rapidly gaining weight and feeling well. He returned four months later with pain in his epigastrium, increasing weakness and loss of weight. There was now a palpable mass in his pyloric region and an infiltration of his abdominal wall—obviously carcinomatous. An X-ray showed the stomach contracted to one-fourth its former dimensions with a complete block at the pylorus and the gastroenterostomy in a contracted state very close to the pylorus and functioning hardly at all. He died six weeks later. At autopsy (Fig. 1) his stomach was small with a mass of the consistency of cartilage infiltrating the pyloric

region and extending along the greater curvature a short distance beyond the gastro-enterostomy, which was now only about two and one-half inches from the pylorus. The gall-bladder was atrophic and there was an abscess containing about four ounces of odorless pus in the right lobe of the liver beneath the gall-bladder. The duodenum was three times its normal size and very tense with fluid. The common duct was an inch across, and tense. The papilla of Vater was wide open and the duct contained no stones. The hepatic ducts were greatly dilated up to their small subdivisions in the liver. The pancreas had been to some degree invaded by the growth which was adherent to its head. The pancreatic duct opened near the orifice of the papilla and did not seem much dilated. The remainder of the pancreas showed no gross lesion and microscopical sections showed no evidence of inflammation.

Acute pancreatitis has always been something of a puzzle. In most instances the classical finding of a gall-stone impacted in the lower ampulla,

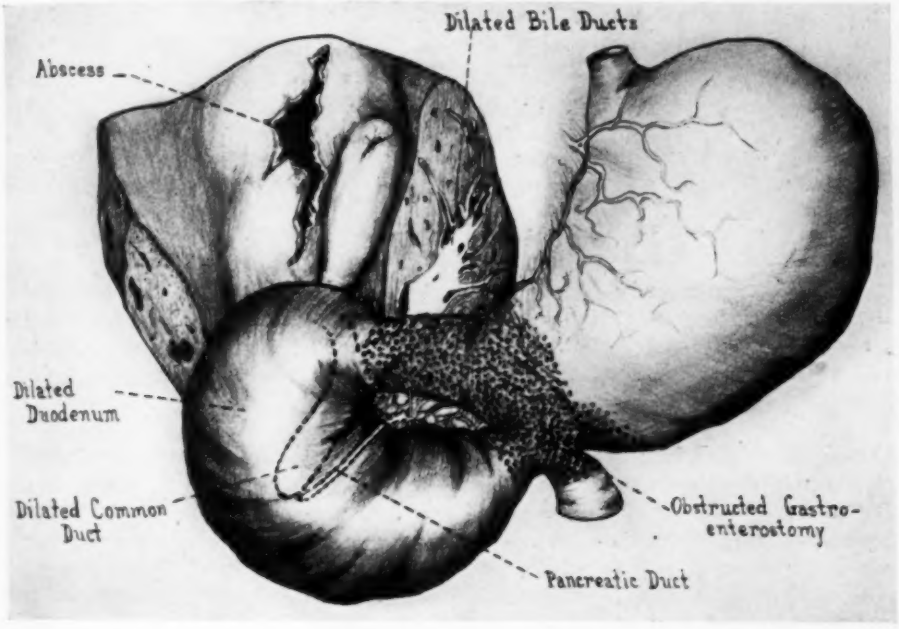

FIG. 1.—Diagrammatic illustration of condition found at autopsy.

as described by Opie, is lacking, but when this has been occasionally found it has been thought by many to be the soundest explanation of its occurrence. Macallum* says regarding it: "The cause was quite obscure until Opie discovered a case in which a small gall-stone had become impacted in the orifice of the ampulla of Vater in such a way that neither bile nor pancreatic juice could escape although bile could run back from the common bile-duct into the pancreatic duct. Opie readily showed that injection of bile into the pancreatic duct would produce acute hæmorrhagic pancreatitis in animals and Flexner showed that gastric juice and many other irritating substances would do so too. He found that fresh bile was most effective, that mucus rendered its action far milder and produced rather chronic effects." The

* Textbook of Pathology, p. 398.

other notions about the cause of acute pancreatitis are not pertinent to this discussion. Here we had developed a hydrostatic pressure from accumulation of biliary pancreatic and duodenal secretions sufficient to dilate the duodenum to three times its normal size, force the sphincter of Oddi, dilate greatly the whole biliary tree and leave the pancreatic duct opening into the duodenal cloaca, so to speak, with free communication back and forth of the fluid containing bile, duodenal secretion and pancreatic juice. No doubt this mixture was less irritating than pure bile. Surely this isolation of the duodenum came about gradually and could not have long been complete but it seems remarkable that acute pancreatitis did not develop.

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BOBBIN ATTACHMENT TO SCISSORS OR NEEDLE-HOLDER FOR LIGATING AND SEWING

FIG. 1.—Shows scissors with bobbin attached to carry ligature material. The long arm of A fits into the tube attached to the scissors, each being flattened on one side. Bobbin B slips on the split short arm of A which provides the proper tension for the former.

Fig. 2.—Needle-holder showing bobbin attachment holding a full tube of catgut. The needle has an eye in the point end with a large guide ring on the other end.

A is a guide tube attached to a two-arm piece. To mount, slip end of tube into ring on needle holder, then pull the lower arm back into short flattened tube on rear of shank. Bobbin B slips on split arm of A. C is a large common needle four inches long used as a shuttle.

To use the scissors with bobbin, the suture is brought through a small hole under the mounting tube. The knot is best tied with the left hand for economy of gut. If much tying is to be done, as in goitre operations, two tubes of ligatures may be wound on the spool or a second bobbin used.

It gives the assistant more time to handle hæmostats and the ligatures and scissors are always together. I have reduced my ligating time 50 per cent. I find that non-boilable catgut, the kinks of which can be eliminated by stretching, is best adapted to this method of tying and suturing.

There are two principles involved in the sewing apparatus. First, broader surfaces are available for healing; second, the strain of the wound is placed more upon the sutures than upon the tissues.

At first glance sewing by this method seems complex, but in reality it is very simple. You have a tube of catgut that will close the average incision. For each layer but one knot is tied, while it is not necessary to attach hæmostats to the peritoneum or fascia for as the suture is introduced the cut edges are drawn into a vertical position, making introduction of the next stitch easy, while the last stitch holds the tissues so securely that they do not slip apart. (See Fig. 3.)

The threaded needle is introduced through the cut edges of the distal end of the peritoneum or fascia. The free end of the catgut is pulled through. It should be about two inches longer than the incision, *i.e.*, it should reach to the opposite end with enough more to allow for tying. A common heavy rug needle three or four inches long should be tied on the free end as a shuttle. The needle is withdrawn and reintroduced about one-quarter inch from the first. By slightly withdrawing the needle the suture will loop so that the shuttle needle in the left hand of the operator can be pushed through the loop

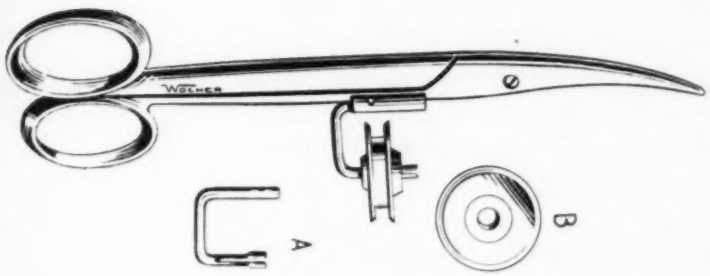

Fig. 1.

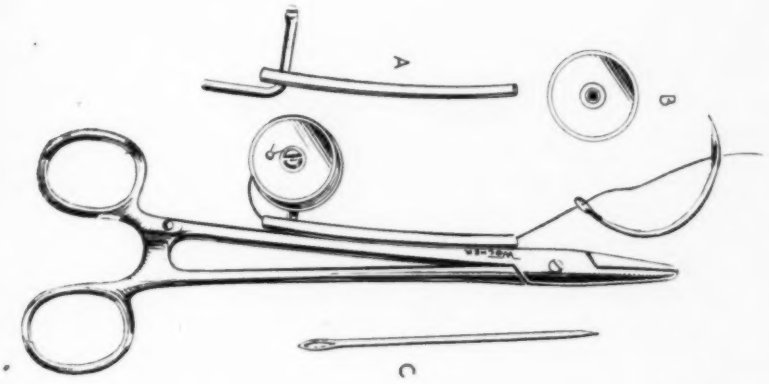

Fig. 2.

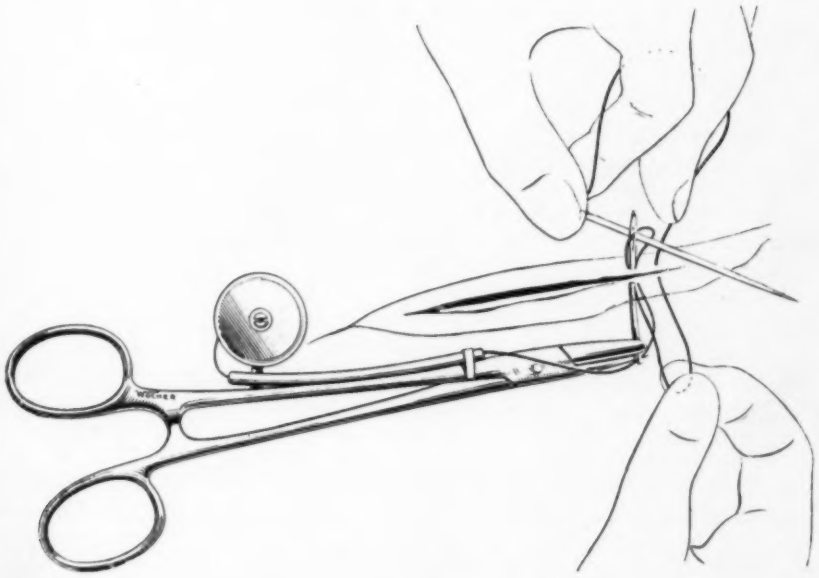

Fig. 3.

on the side distal to the needle. The assistant, I find, should hold his side of the suture lightly between the index finger and thumb of his right hand during the introduction of the needle, and when the needle is withdrawn he takes the suture between the same fingers of the left hand, pulling it parallel with the incision toward the unclosed end. At the same time, the operator pulls the shuttle end of the catgut in the same direction. When the layer is closed, the suture is cut and tied and the next layer closed likewise. If you believe in closing the muscle layer, you can use interrupted sutures with no trouble. *Always pass the shuttle or free end of the gut through the loop distal to the eye of the needle*, otherwise your needle will be caught.

Advantages.—(1) The peritoneum is closed securely with the cut edges extraperitoneally.

(2) The fascial layers have broader surfaces for healing and the cut edges stand up ideally for the introduction of figure-of-eight stay sutures.

(3) It is a fine method for closing the first layer in gall-bladder operations for it prevents the troublesome splitting of the fibres of the transversalis muscle and fascia.

(4) It is a quick and simple method for introducing mattress sutures in operations for umbilical hernia; also for single or double sutures in inguinal hernia.

(5) It is well adapted for skin suture with silk, dermal or catgut. The suture should be placed near the edge for good coaptation; tension of sutures should be avoided in the skin for the suture is hæmostatic. It is quickly and painlessly removed by taking out the straight locking suture and the knot, the other half ravels out instantly.

(6) In pelvic work there is no loose catgut to entangle the hæmostats.

(7) As a hæmostatic stitch, I have tried it on the intestines of animals and find it makes a beautiful and strong anastomosis.

(8) This bobbin can be attached to any kind of scissors or needle-holder. The apparatus can be removed instantly if the operator desires to use the older methods.

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LIPIODOL IN DIAGNOSIS OF RETAINED COMMON BILE-DUCT STONE

IN A previous communication to this journal* a study of lipiodol injections of post-operative biliary fistulæ was reported. In that series we were unable to report visualization of a common-duct stone as such, although, in one instance, the presence of a common-duct stone had been correctly postulated by demonstrating an obstruction at the papilla of Vater. In the present communication Case I is reported, firstly, to supplement the previous series by presenting a plate actually showing a retained common-duct stone, and secondly, to illustrate that variations in quantity of lipiodol injected may affect visualization. Case II is reported to illustrate the type of indirect evidence leading one to suspect the presence of a retained common-duct stone following cholecystostomy.†

Both cases illustrate the feasibility and advisability of performing a cholecystostomy as a first-stage operation in severely ill patients with common-

* ANNALS OF SURGERY, vol. xci, pp. 233–241, February, 1930.

† Cases from the surgical service of Doctor Neuhof, the Mount Sinai Hospital, N. Y. C.

duct obstruction. Prerequisites for this type of operation are of course a patent cystic duct and the presence of bile in the gall-bladder. The nature of the common-duct obstruction can then be fairly accurately determined at a subsequent stage by a lipiodol injection and the appropriate second-stage procedure performed.

CASE I.—E. F., aged sixty-one, was admitted to the surgical service of Doctor Neuhof in May, 1930. For thirty-six hours he had been suffering from violent epigastric

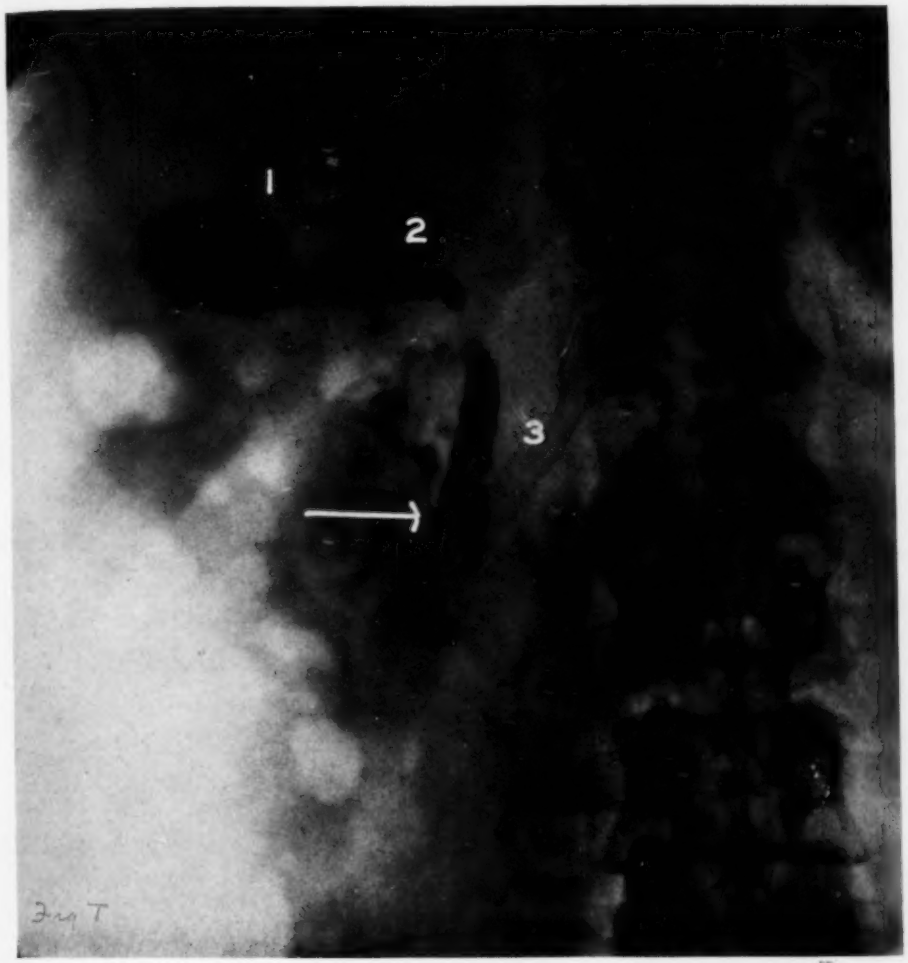

FIG. 1.—Plate taken after the first injection showing a definitely outlined defect in the lipiodol shadow at the lower portion of the common duct, caused by a retained stone.

pain and repeated vomiting. He was suffering intense pain, was markedly prostrated, and had marked right upper quadrant rigidity and tenderness. Under observation for twenty-four hours the patient experienced a chill, prostration became extreme, and a slight icteric tinge appeared in the scleræ. Operation revealed an enlarged, tense, acutely inflamed gall-bladder which, on aspiration, yielded pus and bile. Because of the poor general condition of the patient it was thought inadvisable to do an extensive exploratory

procedure and the operation was accordingly limited to a simple cholecystostomy with evacuation of pus and sandy material.

Three weeks later lipiodol was injected through the cholecystostomy sinus under fluoroscopical control. A radiotransparent area which was gradually encircled by the injected lipiodol could be seen. At the same time lipiodol could be seen entering the duodenum in little trickles, rather than with the rush usually observed.

In September, 1930, patient returned for re-operation and a soft stone was removed in segments from the lower portion of the common duct. The stone could not be felt by external palpation of the common duct through the foramen of Winslow.

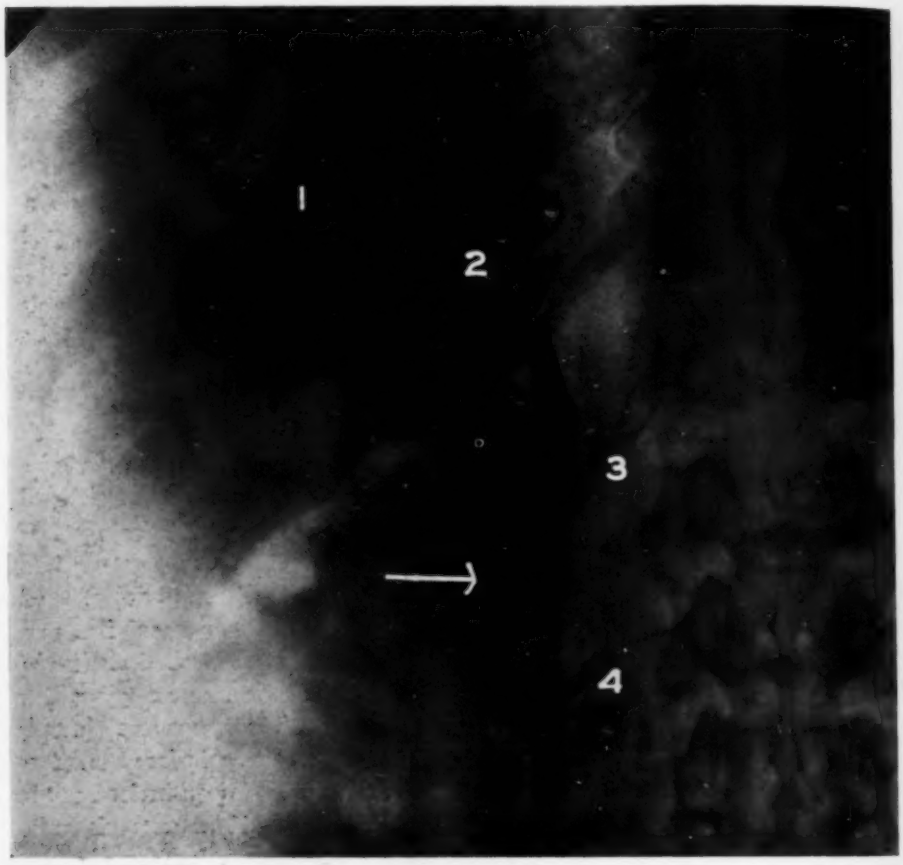

FIG. 2.—Plate taken fifteen minutes later, after the injection of ten cubic centimetres more of lipiodol. The defect caused by the stone is obscured by the shadow of the increased quantity of lipiodol. The retention of the lipiodol in the common duct and its slow emptying are indicative of obstruction. The arrow points to the common-duct stone. 1—Gall-bladder. 2—Cystic duct. 3—Common duct. 4—Lipiodol trickling into the duodenum.

CASE II.—E. M., aged sixty-three, was admitted to the Mount Sinai Hospital in January, 1931. One year ago she had been operated on for a toxic thyroid adenoma. She had been known to have high blood-pressure, as high as 230, systolic, for a number of years. She also had symptoms and electrocardiographical findings of coronary artery disease. During the past year she had experienced a number of severe attacks of biliary colic with a rise in temperature to 104°, chills, and jaundice. Following one of these attacks she was admitted to the Mount Sinai Hospital with a temperature of 104° and tenderness and rigidity in the right lower quadrant. Stool contained bile and the icteric

index was only slightly raised. Her symptoms did not abate. Cholecystostomy was performed under local anæsthesia. The gall-bladder contained bile which was clear at the fundal portion and purulent near the neck. Because of the poor condition of the patient the operation was limited to removal of the gall-bladder stones and the performance of a cholecystostomy.

Six weeks later lipiodol was injected through a very narrow biliary fistula. Under

FIG. 3.—Case II.—Plate taken eighteen hours after lipiodol injection into the gall-bladder. The ascent of lipiodol into the intrahepatic radicles and its presence in the intestine indicates the presence of an incomplete obstruction in the common duct. The failure to visualize the common duct at the time of exposure indicates that the obstruction is relieved intermittently. 1—Gall-bladder. 2—Cystic duct. 3—Intra-hepatic biliary radicles. 4—Lipiodol in ileum.

fluoroscopical control 25 cubic centimetres of iodized oil were injected. The gall-bladder and cystic duct became gradually distended and peristaltic action could be observed. However, no oil was seen to enter the common duct, even after half an hour. A plate taken eighteen hours later, however, revealed the presence of lipiodol in some of the

intrahepatic biliary radicles of the right lobe. Lipiodol was also seen in the intestine. Forty-eight-hour plate showed the same condition. Seventy-two-hour plates showed the gall-bladder empty and the lipiodol had by this time disappeared from the biliary radicles. At no time was the common duct seen. From previous experience it was felt that the ascent of lipiodol into the intrahepatic radicles was indicative of an obstruction below the junction of the cystic and common ducts. The presence of lipiodol in the intestine indicated that the obstruction was incomplete. The failure to visualize the common duct indicated that the obstruction was intermittent in character. The most likely cause of such an intermittent obstruction was taken to be a ball-valve calculus. Operation revealed a very freely movable stone the size of an olive pit in the common duct.

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A CORK ADJUVANT TO THE MURPHY BUTTON

THE Murphy button for intestinal union as developed by Dr. John B. Murphy, in 1892, received general acclaim, but, lately, the strong interest and frequent use of the Murphy buttons has waned considerably. This is probably due more to our improved sewing materials, careful asepsis, and better methods of intestinal anastomosis by suture than to any inherent faults of the button itself.

However, there are special situations and locations for intestinal union where the button continues to serve best and has advantages over any type of suture anastomosis when estimated on a basis of speed, safety, and simplicity.

Regularly, the writers had preferred and employed it after difficult subtotal gastrectomies. Here we favor and perform a gastroenterostomy of the anterior type. To this long-loop type of anastomosis is added the necessary and important jejuno-jejunostomy between the limbs of the attached jejunum. This lateral anastomosis is rapidly and reliably accomplished with a Murphy button. After the completion of the posterior portion of the gastrojejunostomy, and before the anterior part of the stoma is closed, the separate hemispheres of the Murphy button are placed into the open limbs of the hooked-up jejunum. They are allowed to rest about four to five inches below the stoma. Each bowl of the button is so held that the cylinder thereof is firmly pressed against the anti-mesenteric border of the bowel. (Fig. 1.) This tensed diaphragm of gut is then incised crucially with a narrow scalpel to permit the cylinder to extrude through a small opening. An ordinary bottle cork previously fitted and of proper size is then quickly inserted into the hollow stem or cylinder (Fig. 2) to prevent intestinal leakage and to fix the button *in situ*, so that it cannot slip upward or downward, inward or outward.

Although only one select opportunity is here described in detail, any anastomotic demand that is best accomplished with the round Murphy button, *e.g.*, cholecyst-gastrostomy and ileo-colostomy, may be made more facile in its technical performance by utilizing the cork procedure.

Fig. 1.—a.—The cylinder of the Murphy button is forced against the anti-mesenteric border of the jejunum. A small crucial incision is made into the tense diaphragm of gut. b.—The stem of the hemisphere is extruded and the fitted cork is inserted therein.

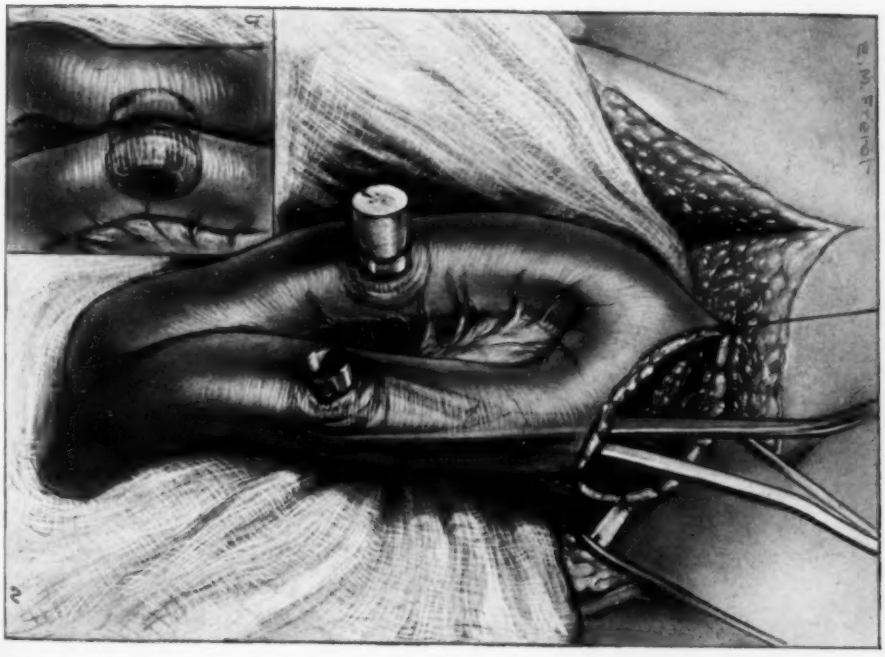

Fig. 2.—a.—The cork in the stem of the Murphy button prevents it from slipping out of position, otherwise the fingers or a long clamp must hold it in place. b.—The halves of the Murphy button in completed position.

The cork serves as a useful handle for the button, since it is easier to control than most special holding or ordinary clamps that are employed to steady or maintain the device while it is adjusted into its desired position.

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